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# GELATINOUS CARCINOMA OF THE BREAST[1]

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ONE reason why the breast has been called the mother of surgical pathology is the protean character of mammary cancer. Although cancer of the breast is basically a disease entity, it is really not one but many diseases. The diffuse duct carcinoma, the bulky adenocarcinoma, the intracystic or intraductal papillary carcinoma, the acute inflammatory carcinoma, the sweat gland carcinoma and Paget's cancer are all varieties of mammary cancer, yet they differ greatly in their clinical and pathological characteristics. A rare and interesting subvariety is the gelatinous carcinoma of which we have had the opportunity of studying 30 cases.

Gelatinous degeneration of tumors has long been of speculative interest, since 1816 when Otto first described gelatiniform carcinoma of the stomach. The first accurate histological study was made by Johannes Mueller. Gelatinous degeneration is more common in malignant neoplasms of the digestive tract and generally occurs in regions covered over in the normal state by an epithelium which secretes mucus. Its occurrence in the breast is rare and excites interest because this organ does not normally secrete mucus, nor are its cells mucigenic in appearance. The gelatinous carcinomata of organs other than the breast, e.g., of the rectum and stomach, have a relatively low degree of malignancy, growing slowly and metastasizing late in their course. In this respect they resemble the gelatinous carcinomata of the breast.

Gelatinous carcinoma has been variously named, as gelatiniform carcinoma (Billroth), carcinoma myxomatodes (Dixon), myxoid carcinoma, mucoid or mucous carcinoma, colloid carcinoma, carcinoma gelatinosum, and carcinoma mucosum. The term "colloid" cancer should be abandoned in favor of "gelatinous" carcinoma, which designation is more truly descriptive.

## INCIDENCE

Gelatinous carcinoma is a rare variety of mammary cancer. The incidence is uniformly given by many authors as 1 to 2 per cent of all cancers of the breast. We were able to discover only 30 (1.56 per cent) gelatinous carcinomata in a histological review of 1922

TABLE I.—INCIDENCE OF GELATINOUS CARCINOMA IN THE BREAST

| | Per Cent |
|---|---|
| Gaabe: 49 in 2,944 mammary cancers | 1.66 |
| Lange: 17 in 1,814 mammary cancers | 0.93 |
| Lee, Hauser, and Pack: 30 in 1,922 mammary cancers (personal cases) | 1.56 |
| Lee, Hauser, and Pack: 144 in 10,355 mammary cancers (collected cases) | 1.39 |
| Lewis and Reinhoff: 12 in 950 mammary cancers | 1.3 |
| Malherbe: 7 in 326 mammary cancers | 2.14 |
| Schmidt: 1 in 82 mammary cancers | 1.22 |
| Simmonds: 4 in 1,200 mammary cancers | 0.33 |
| Spangenthal: 20 in 638 mammary cancers | 3.13 |
| Stout | 1.1 |
| Warren and Witham: 3 in 162 mammary cancers | 1.85 |

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mammary cancers. Cheatle and Cutler believe this tumor to be more common than generally supposed, basing their conviction on the use of whole serial sections of the breast and so discovering gelatinous degeneration in tumors in which its presence was totally unsuspected. In our opinion the purely gelatinous carcinomata, recognized grossly as such, are of great rarity, although gelatinous degeneration of parts of any of the varieties of breast cancers may not be so infrequent.

### CLASSIFICATION

Gelatinous carcinomata of the breast are logically subdivided into two distinct groups based on physical findings, clinical course, gross and microscopic pathological anatomy.

1. *Primary gelatinous carcinoma in which the gelatinous features predominate.* The gelatinous element presumably arises *de novo* with the onset of malignancy in a pre-existing papillary cystadenoma. This type occurs usually in patients of advanced age. It is of extremely slow growth and may exist many years before it is suspected to be carcinomatous. The absence of skin adherence and nipple retraction, the encapsulation of the tumor, and the infrequency of metastasis confirm the relative benignity of this variety of mammary cancer. The tumor has the gross appearance of a gelatinous or mucous cyst and under the microscope the epithelial elements are few and scattered. These encapsulated gelatinous carcinomata have sometimes been cured by local excision, although this treatment is not recommended as a routine procedure.

2. *Ordinary carcinoma of the breast with secondary gelatinous degeneration.* The bulky adenocarcinoma of the breast, which has a tendency to undergo spontaneous degenerative changes, is the histological type most frequently involved; the ductal carcinomata may show similar though less marked gelatinous changes. The gelatinous character of the tumor may or may not be grossly discernible. It may be recognized in some tumors only by microscopic examination and then found to involve only a portion of the carcinoma. We have the impression that the gelatinous degeneration is an incidental occurrence in these cancers, which may retain their full degree of malignancy. We have observed gelatinous degeneration in a carcinoma of the breast, in which other parts were anaplastic and highly malignant (Fig. 4). This group of gelatinous carcinomata of the breast have no distinguishing clinical or pathological characteristics. They may occur in patients of all ages; the rate of growth, degree of malignancy, tendency to metastasize, and physical signs produced are the same as for ordinary mammary cancers of the same histological classification. The gelatinous degeneration originates in either the connective tissue or epithelial elements of the tumor, or both. This origin cannot be determined in many cases. These subdivisions have been classified as follows:

a. *Myxoid carcinoma.* A variety of gelatinous carcinoma of the breast in which the gelatinous changes arise by metaplasia in the connective tissue, i.e., it becomes myxomatous.

b. *Mucoid carcinoma.* A variety of gelatinous carcinoma of the breast in which the gelatinous material originates directly from the carcinoma cells.

### GROSS PATHOLOGICAL ANATOMY

The classification which we have adopted for gelatinous carcinomata of the breast takes full cognizance of the marked difference in the gross appearance of these tumors. The type classified as showing secondary gelatinous degeneration in any of the histological varieties of mammary cancer, has practically no distinguishing gross characteristics. The wholly gelatinous carcinomata of the breast on the other hand constitute a definite clinicopathological entity. We shall confine our description largely to the encapsulated, purely gelatinous tumor.

The encapsulation of the tumor and the freedom of the skin, nipple, and breast fat from invasion after years of growth may confuse the diagnostician. Ewing states that the small and wholly gelatinous neoplasms in the breast may be mistaken for simple mucous cysts and their carcinomatous character may be overlooked. To the naked eye, such a tumor may be readily confused with myxoma.

A cross section of these round, nodular tumors may reveal numerous tiny concretion-

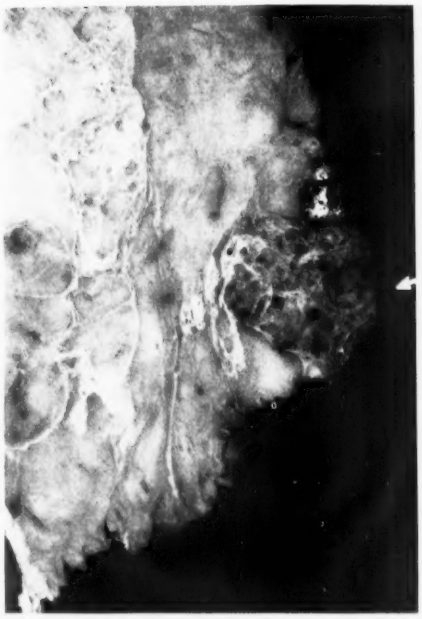

Fig. 1. Encapsulated multilocular gelatinous carcinoma of the breast. The tumor is intersected by thin fibrous strands to form compartments of variable size.

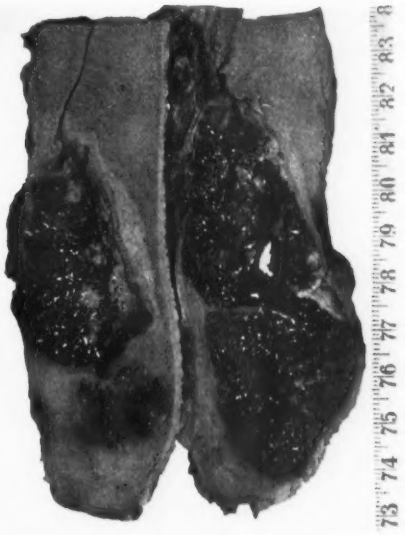

Fig. 2. Hæmorrhage and liquefaction necrosis in a gelatinous carcinoma of the breast. The locules are small and the tumor exhibits greater growth activity than the specimen seen in Figure 1. It is partially encapsulated but is adherent to the pectoral muscles.

especially in the center of the cancer, which may resemble the corpora amylacea of the prostate and are seldom larger than 130 micra in diameter (Olivier). The contents of the encapsulated tumor are juicy and gum-like with the consistence of firm jelly, trembling on the knife. The gelatinous substance is not fluid enough to flow but it can be readily extruded from the locules, by gentle pressure between the thumb and finger.

The color of the tumor is variable depending on its vascularity and the presence or absence of degenerative changes. The pure gelatinous content is a lustrous, light greenish-gray or occasionally yellow, but if hæmorrhage and fatty metamorphosis occur, the gelatin assumes an opaque dull brown appearance. Some of the tumors have been described as pearly, pink, pale orange, wine, or chocolate color, resembling coagulated blood. When a thin cross section of the tumor is held to the light it may resemble a section from a colloid goiter (Reel). Numerous small blood vessels can be seen ramifying in the delicate walls of the large and small locules, a factor which contributes to the frequency of hæmorrhagic changes in the tumor and variance of color from pink to chocolate. This is one of the chief points of difference between gelatinous cancers of the breast and of other organs, such as the stomach. The grayish, gelatinous tumors may contain small reddish-brown hæmorrhagic spots throughout their substance, thus rendering them less translucent than normal.

The tumor is intersected or honeycombed with thin fibrous strands of white trabeculæ, disposed in a reticular arrangement, forming meshes or compartments of variable size (Fig. 1). The presence of this cloistering of the tumor into locules or loges is uniform in this variety of gelatinous carcinoma. The connective tissue septa may also be translucent and occasionally myxoid. The cystic cavities are lined with a smooth thin membrane. The individual locules vary in size from 1 millimeter to 1 centimeter (pin-head to pea). The larger tumors have correspondingly larger

Fig. 3. Gelatinous degeneration of a bulky cystadenocarcinoma.

cavities. The center of the tumor is the most nodular portion and toward the periphery the nodules or locules become smaller and more opaque (Fig. 2).

PATHOLOGICAL HISTOLOGY

The gelatinous carcinomata are found usually in the group of bulky adenocarcinomata and intracystic papillary carcinomata and less frequently in the ductal and small round cell carcinomata of the breast. The gelatinous element may so dominate the microscopical picture that the particular histological type of cancer is obscured.

The epithelial cells comprising the carcinoma show great variability in size depending on their location in the tumor and the degree of degeneration. Some of the degenerating cells contain mucin in small transparent droplets (Fig. 7), while other cells are so distended by the mucin that the remnant of nucleus is barely visible. The translucent intracellular mucin occupies more space than the unaltered protoplasm which no doubt accounts for the globular swelling of these cells. Other cells are oval and contain atypical, large, ovoid or spherical nuclei; we have not observed the elongated nuclei which Lebert characterized as typical. Cells with arborescent nuclei are occasionally found in the center of the cell nests. The younger cells in the outer or marginal gelatinous locules have many nuclei, and most of the cell content is comprised of nuclei. The older cells are paler and have ill defined borders. The cytoplasm of the epithelial cells often seems hyaline but in other cases is involved in granular and fatty degeneration.

In the typical or wholly gelatinous cancer of the breast, the minute architecture of the tumor is so distorted that no well defined picture can be painted. The cells may appear in cylindromatous arrangement or in isolated tubular or alveolar islands in a sea of mucus. These tubules or alveoli may be distended with mucus while others appear as inactive, well differentiated, and well preserved epithelial clusters. The membrana propria of the acini and ducts is early destroyed. The cells are still preserved in some locules, in others they are disappearing, and finally in others they have completely disintegrated, leaving only cellular skeletons in the center of the lobule (Fig. 6). In the oldest loculi, the content is almost exclusively mucus with little or no trace of the carcinoma cells. Larrey reported the case of a recurrent mammary cancer weighing 2,300 grams, which was completely gelatinous as no cancer cells could be found on microscopical examination. As a rule some epithelial cells can be found if diligent search be made. These cells are separated from the connective tissue stroma by the intervening mucus. The degeneration of these cells is seemingly due not only to pressure atrophy by the mucus but also to their isolation from a nutritive source and possible in

terference with the process of diffusion by the enveloping œdematous mucus.

The gelatinous layer is smaller in the peripheral layer or margin of the tumor, and is most abundant in the older acellular central part. The typical gelatinous carcinoma of the breast is carcinomatous only in its peripheral portion with its center containing only relatively benign, i.e., gelatinous elements. The process of growth of the cancer occurs only at the periphery, where active carcinomatous tubules and alveoli may nearly always be found, although degenerative changes occasionally may be seen here before any mucin is visible. A similar condition is found in the axillary lymph nodes; the center of the node may be completely invaded and replaced by mucus, while its periphery contains actively growing carcinoma. Some of the lymphatic channels of the superficial cutis may be filled with gelatin.

The mucus may be disposed in delicate strands, which become filiform in the older segments of the tumor before they disintegrate completely. The presence of mucin in the tissues seems to cause no reaction in the majority of these tumors, although Doutrelepont and we independently have observed occasional lymphocytic infiltration surrounding the gelatinous locules (Fig. 12). Wells injected rabbits with large quantities of pure tendon mucin almost daily for 2 to 4 months, and showed absolutely no deleterious effects, either locally or constitutionally. The calcareous deposits, fatty changes, and occasional hyaline bodies are considered coincidental and unimportant.

The infrequent gelatinous metamorphosis of breast cancer, known as the connective tissue type or myxoid carcinoma of the breast, has been described best by Philip Reel as follows: Some carcinomata of the breast with abundant connective tissue framework present great quantities of mucinous intercellular substance which seems to extend widely into the tissue space of the tumor stroma. The stroma of the tumor is of homogeneous, translucent, mucoid material containing spindle, stellate, and round connective tissue cells, but staining poorly with ordinary dyes. The collagen fibers are swollen and separated by fluid

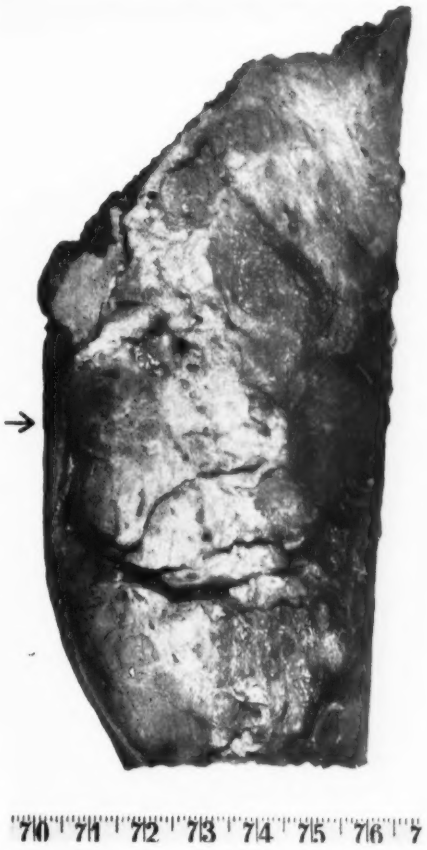

Fig. 4. Small focus of gelatinous carcinoma occurring as a secondary change in a large adenocarcinoma of the breast.

so that the cells present a water soaked appearance. While the blood supply is usually described as poor, Reel states that his specimens show a rather large number of moderately dilated blood vessels, having thin and poorly developed walls. He considers the possibility that the resulting stasis indicates a disturbance that is responsible for this type of degeneration. The epithelial elements or carcinoma cells proper are not directly involved in this process.

*Nature of gelatinous degeneration.* The appearance of mucus in the cells of the gastrointestinal mucosa would be considered a normal physiological procedure, in which the mucus merely becomes visible by an increase

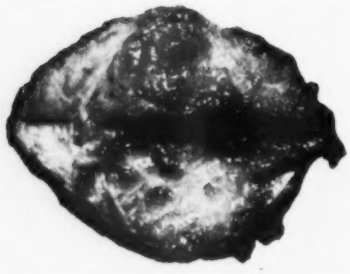

Fig. 5. Gelatinous carcinoma of the breast in which the stroma of the tumor is involved in myxomatous degeneration.

in the specific secretory activity of these cells. In the case of neoplasms, when the mucus becomes excessive and permanent the condition is no longer physiological but pathological and is termed gelatinous degeneration. Mucin as it appears in a degenerative change, imbibes water, swells, and acquires its characteristic turbid or colloid appearance. The occurrence of gelatinous degeneration in carcinomata of the breast is still more remarkable, as the mammary gland does not normally secrete mucus. The character of the changes occurring in the carcinoma cells of the breast is unknown, but apparently some of the gelatin originates in the cytoplasm of the cell. The disintegration of the cells cannot be attributed entirely to this conversion of cytoplasm into mucin but is due in part to nutritional disturbances brought about by the pressure of the gelatinous material upon these cells. The connective tissue type of mucoid degeneration seems to be a reversion to the fetal or embryonal type of connective tissue, resembling the myxomatous Wharton's jelly of the umbilical cord and is characterized by an excessive accumulation of a liquid mucinous intercellular substance. The cause of these degenerative changes remains a cryptic problem.

*Origin of the gel.* Mucin occurs in two locations in the normal body; as a product of the secretory activity of epithelial cells, e.g., the salivary glands and the digestive tract, and also in the interstices of connective tissue, e.g., tendon. Both epithelial and connective tissue mucin may occur in the breast under certain conditions notably in association with neoplasms. We need only to recall the existence of a layer of mucous connective tissue immediately around the ducts and acini in the normal gland to find an explanation of the occurrence of myxoid metamorphosis of the stroma of cancer of the breast. This connective tissue mucin is more obviously recognized in such breast tumors as the periductal myxoma of Warren and the cystosarcoma phyllodes mammæ of Johannes Mueller. The most singular fact about these degenerative changes is that the epithelial cells of the breast do not normally secrete mucin, therefore the presence of gelatinous changes in the cells of mammary carcinoma is a unique metamorphosis, quite unnatural when compared to the gelatinous carcinomata of the gastrointestinal system. We shall not attempt to settle the controversy concerning the epithelial or connective tissue origin of the gel found in gelatinous carcinomata of the breast. Our studies indicate that the epithelial cells, i.e., the carcinoma cells *per se*, are the source of this material in the majority of cases. Less frequently, the stroma of the cancer may independently assume myxoid characteristics, but in this case the mucin is part of a fixed, cellular, organized tissue and not a free exudate. The opinions of various investigators are adumbrated in Table II.

TABLE II.—ORIGIN OF MUCIN IN GELATINOUS CARCINOMA OF THE BREAST

| Origin | Supported by |
|---|---|
| a. Epithelial | Aschoff, Cheatle and Cuthler, Cornil, del Rio, Doutrelepont, Klebs, Ribbert, Rindfleisch, Rubenson, Shaut, Virchow, Wagner, Ziegler, Zimmermann. |
| b. Connective tissue | Lange, Meyer |
| c. Epithelial or connective tissue, either or both | Borst, Ewing, Foerster, Kaufmann, Moeller, Muggenthaler, Scheiffel, Schmittmann, Simmons |
| d. Vascular | Doutrelepont, Koester |
| e. Fat tissue (occasional) | Ewing |

Fig. 6. Low power photomicrograph to show the disposition of the gelatinous locules at the periphery of the breast between normal breast tissue, *A*, and fat, *B*. The epithelial cells of the tumor are seen as numerous small islands in a sea of mucus. The capsule is thin and insecure.

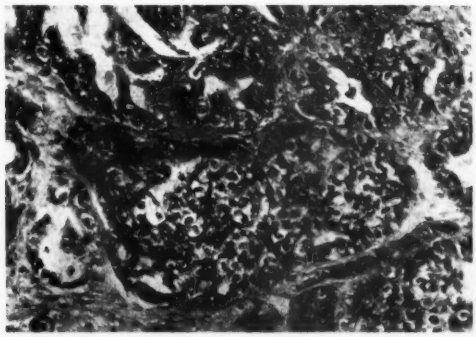

Fig. 7. Early gelatinous degeneration in a bulky adenocarcinoma of the breast. Some of the degenerating cells contain mucin in small transparent droplets, while other cells are so distended by mucin that the remnants of the nuclei are barely visible.

It is our opinion that the majority of gelatinous carcinomata of the breast reveal histological evidence of the epithelial origin of the mucin. The ducts and alveoli of adenomata and carcinomata are sometimes seen to be distended with mucus (Fig. 10); this finding suggests that in the beginning the process is secretory rather than degenerative. The ductal cells are compressed flatly against the basement membrane. According to Ribbert, the mucus ruptures through to the connective tissue spaces where it absorbs fluid and causes œdema (gelatinous imbibition). If this is true, as we have every reason to believe, the stroma of the cancer may be infiltrated both by the released mucus and again by the carcinoma cells producing the mucus, therefore the discovery of this gelatinous substance in the connective tissue does not prove its origin from this tissue nor does the peripheral or central position of the carcinoma cells determine the genesis of the gel. The quantity of mucus may be so abundant and the number of epithelial cells so few that this relationship may be questionable, but always, if diligent search be made, the association of carcinoma cells in the mucus is found. The epithelial origin of the mucus is seldom disputed in gelatinous carcinomata of the stomach and rectum, where the paucity of carcinoma cells is the usual finding. The appearance of gelatin in the axillary lymph nodes containing metastatic carcinoma from the breast is presumptive evidence of the epithelial origin, unless we could assume that both the epithelial and connective tissue elements of the cancer have metastasized together, or that some chemical agent traveling with the metastasizing cells causes the stroma of the nodes to undergo mucinous changes. This would seem unlikely as the malignant connective tissue tumors of the breast seldom metastasize to axillary nodes.

In the myxomatous degeneration of breast tumors (periductal myxoma, cystosarcoma phyllodes, myxoid carcinoma), the mucous tissue is really a firm, resistant, immovable tissue with fixed cells and capillaries. This mucin does not extrude nor is it readily expressed from the cut surface of these tumors. as it is in the true gelatinous carcinomata of the breast. Here the normal stroma of the tumor is substituted by a true mucous tissue which in turn degenerates into a dead mucous tissue (Meyer). This myxomatous connective tissue accompanying mammary cancer is genetically and microscopically similar to that found in myxœdema and certain neurogenic tumors, but quite dissimilar to the mucus occurring in true gelatinous mammary cancers.

Ewing has presented the only logical arguments in favor of the connective tissue origin of the gel, although he believes in the dual genesis. Ewing states that he has occasionally seen compact alveoli lying in broad areas of mucous stroma with no evidence of mucous

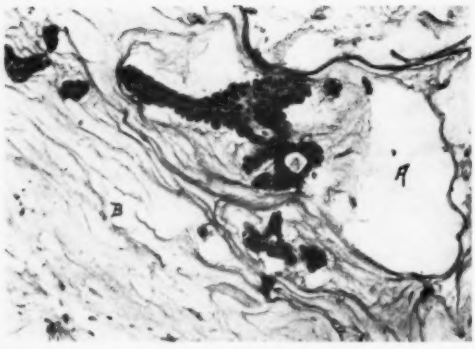


Fig. 8. The carcinoma cells seen in this illustration formerly lined the alveolus, the outline of which is seen at *A*. The alveolus has ruptured and the carcinoma cells and gelatinous material *B* as well have infiltrated the surrounding connective tissue.

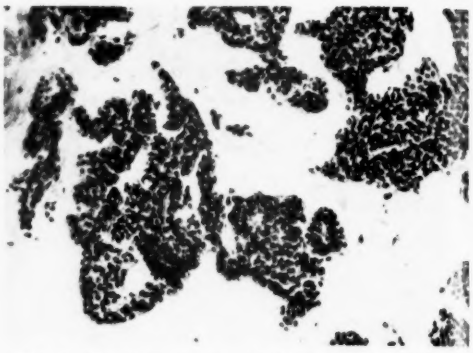

Fig. 9. Compact groups of well preserved carcinom cells surrounded by thick mucin. The cells are of unifor size and exhibit only slight evidence of degeneration, a though removed from their blood supply.

degeneration of the epithelium. Furthermore, "The usual position of the mucus outside of and surrounding compact groups of well preserved cells is not in accordance with an epithelial origin and has not been satisfactorily explained by those who maintain this origin" (Fig. 9).

As we have seen it, the gelatin is first deposited around the cell nests and infiltrates peripherally to involve the connective tissue layer by layer (Fig. 11). The epithelial cells disintegrate as the mucus increases in quantity, i.e., the cancer cells disintegrate in proportion to the quantity of mucus and this disappearance of the cancer cells begins in the center of the cell nests. This does not necessarily imply that the cytoplasm of these epithelial cells is uniformly converted into mucin, in fact the disintegration seems to be due largely to the pressure of the secreted mucin upon the confined cells. Compact well differentiated alveoli are the last to be spared.

The fat tissue of the stroma of some of the gelatinous mammary cancers shows degenerative mucinous changes, which has led Ewing to conclude that the fat tissue may be the origin of the mucin in some of these neoplasms.

### RATE OF GROWTH

The carcinomata of the breast which have only partially undergone gelatinous degeneration, grow and metastasize as rapidly as their unaffected congeners. Their course is not modified by the accident of gelatinous de generation, so long as fully viable unaltere carcinoma is present. When the entire tumo is gelatinous, especially in the type which w have classified as the purely gelatinous ca cinoma, the rate of growth is slow, the cours of long duration, and the malignancy of lo degree. The literature on this subject is re plete with numerous examples of this slo course. To quote a few of the interesting ob servations:

Gaabe found the rate of growth of gelati nous carcinoma to be only 40 per cent as fas as for ordinary mammary cancers. He re corded the average duration of the tumor be fore operation as 31 months compared with 13 months for ordinary breast cancers. Twelve of Gaabe's patients were aware of the presence of the tumor for 5 or more years before admission to the hospital. Warren and Witham give the total duration from the onset of symptoms until death as 3 years for ordinary breast cancers and 8 years for gelatinous carcinomata, and an average duration before treatment of 4 years for the gelatinous carcinomata. Lange, also, in his summary of 75 cases showed that the total duration of the gelatinous cancers was twice as long as the average carcinoma of the breast. Four of the 20 patients surveyed by Simmonds died without operation but had the tumor from 11 to 14 years, compared with an average duration of life for ordinary mammary cancer

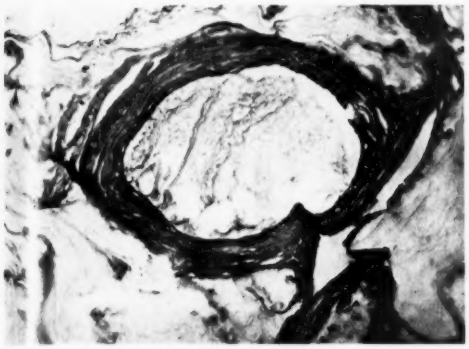

Fig. 10. An alveolus of the cancer is distended by mucus. The epithelium is compressed into a flat single-cell layer. The tissue spaces surrounding this alveolus are infiltrated by the gel. This finding tends to substantiate the epithelial origin of the mucin.

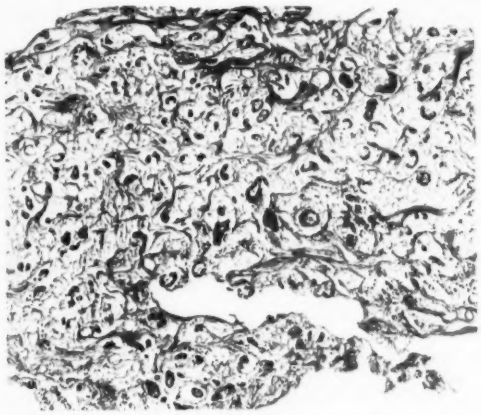

Fig. 11. Infiltration of stroma of cancer by gelatinous material which is always accompanied by a few carcinoma cells usually in small clusters. Epithelial cells stained by hæmatoxylin, connective tissue by carmine, and mucin by blue thionin.

(without operation) of 27 to 32 months. The gelatinous cancer in Olivier's patient was still encapsulated after 9 years' growth. In Dixon's case, the tumor had its onset when patient was 30 years of age, developed an increased growth impetus at the menopause, and was not removed until the patient was 81 years of age, i.e., 51 years after the known date of onset of the tumor.

Ewing attributes the slow growth to the comparative adenomatous structure of these carcinomata and to the mucoid changes in the stroma which interfere with nutrition. Ewing suggests that the long initial, quiescent period is due to the fact that the gelatinous carcinomata originate through the transformation of pre-existing mammary adenomata. It does seem unlikely that a carcinoma could exist and grow so slowly, as these numerous case reports would attest. The tumor is presumably benign (adenomatous) during the first part of its course. The sudden increase in size so often observed may mark the onset of gelatinous degeneration in the cancer rather than indicate an increased impetus of growth, just as occurs in cystosarcoma phyllodes when it originates by myxomatous changes in the stroma of an intracanalicular fibro-adenoma. The average duration of the gelatinous cancers in our series from the recognized date of onset until patient was admitted to the hospital was 20 months, although one patient asserted that it had been present for 8 years.

There have been exceptions to this conclusion that the gelatinous carcinomata are of relatively slow growth. Depres, Critchett, Lister, Stout, G. B. Schmidt, and Cheatle and Cutler have seen gelatinous carcinomata with an especially rapid course.

### DEGREE OF MALIGNANCY

Cheatle and Cutler believe that "gelatinous degeneration is one of the secondary and adventitious changes that may occur in the course of any carcinoma and does not necessarily determine the degree of malignancy of the tumor. . . . The clinical course is dependent on the precise biological properties of the epithelial elements they contain and does not depend on either the presence or the extent of the gelatinous degeneration." Their opinion seems substantiated by the fact that 5 of their 10 gelatinous carcinomata were highly malignant, anaplastic tumors, recurring promptly, metastasizing widely and pursuing a rapid course, but a careful scrutiny of their illustrations reveals that they have used only cases with gelatinous degeneration in parts of the tumor and not the true encapsulated wholly gelatinous carcinomata. As we previously stated in our classification, the ordinary carcinomata of the breast with secondary gelatinous degeneration have the same

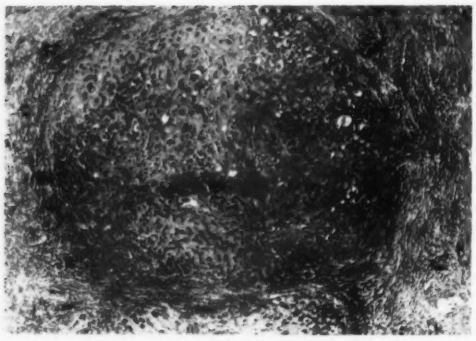

Fig. 12. Lymphocytic infiltration surrounding a focus of gelatinous carcinoma. The margin of the tumor shows the greatest growth activity, where the cells are more abundant and the gelatinous material less homogeneous.

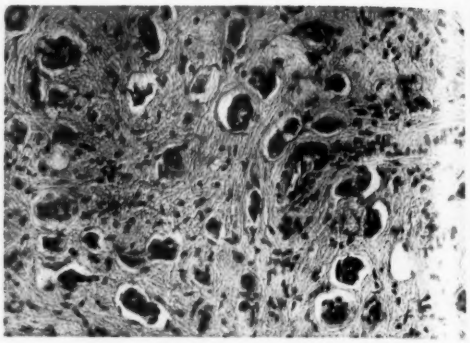

Fig. 13. Gelatinous carcinoma of the breast with cel[illegible] and early myxomatous changes in the stroma of the tu[illegible].

rate of growth, degree of malignancy, and tendency to metastasize as other mammary cancers of the same histological type. But the wholly gelatinous multilocular encysted carcinoma of the breast is a definite clinical and pathological entity, and as such is characterized by a slow rate of growth, late involvement of regional lymph nodes, and delayed recurrence, all of which indicate its low degree of malignancy.

The end-results in our series of 30 cases have influenced us in our belief that the average gelatinous carcinoma of the breast has a low degree of malignancy, e.g., 57 per cent 5 year cures, compared with 41 per cent in a control group of 217 cases of ordinary mammary cancer treated by similar methods. Gaabe reported 58 per cent of his patients clinically free of gelatinous cancer 3 years after treatment, which in his experience was twice as good as the results obtained for ordinary mammary cancer. One of our patients (Case 1) developed a recurrent gelatinous cancer, 25 years after a radical mastectomy. The average duration of life in our fatal inoperable cases was 4.8 years which is another convincing proof of the low degree of malignancy of these tumors.

CASE 1. Gelatinous carcinoma of the breast recurrent after 25 years.

J. C., a white woman, 65 years of age, entered the Memorial Hospital on April 1, 1926, for treatment of a "sore" on her nose (squamous carcinoma). A right radical mastectomy had been done for carcinoma, 25 years before in another hospital. At the present admission, a subcutaneous, movable, ov[illegible] smooth nodule, measuring 1 centimeter in diam[illegible], was found on the chest wall below the scar. [illegible] small tumor was excised on January 7, 1927, the pathological report being typical gelatinous ad[illegible] carcinoma. A postoperative radium treatment [illegible] given to the tumor site on February 4, 1927. The following factors were employed: a radon tray, w[illegible] a radium skin distance of 3 centimeters, a filter of 2 millimeters of brass, and a dose of 3,000 millic[illegible] hours. There was no evidence of carcinoma at the last observation 6½ years later (July 11, 1933).

AGE

The average age of 2,663 patients with ordinary mammary cancer who applied to the Memorial Hospital was 51 years, as compared with an average of 52 years for the 30 patients with gelatinous carcinoma of the breast. The oldest patient with any type of mammary cancer was 90 years and the youngest 17 years, while the oldest patient with gelatinous carcinoma of the breast was 85 years and the youngest 34 years of age. The diagnosis was "primary inoperable" in the former case and "primary operable" in the latter. The average age of the patients mentioned in 94 case reports from other sources was 57 years. It has frequently been asserted that gelatinous carcinomata of the breast occur in relatively older individuals (Kaufmann, Spangenthal). This difference in opinion and fact, perhaps can be attributed to the number of years intervening between the average age at the recognized time of onset of the tumor and the average age of the date of application for treatment. The latter age is not alwa[illegible]

proper in considering the age distribution of gelatinous carcinomata of the breast, as many patients have been aware of the presence of this tumor for 5, 10, and even 12 years before presenting themselves for treatment. The gelatinous degeneration of tumors is not peculiar to old age but is related entirely to phenomena intrinsic to the tumor.

### SEX

Our 30 patients and the 94 patients in case reports collected from literature were women. Graabe found 4 men in his collected group of 84 gelatinous carcinomata of the breast (5.8 per cent). The incidence of ordinary mammary cancers in males at the Memorial Hospital was 1.24 per cent (2,663 cases).

### RACE

The distribution of these patients according to racial origin is of no particular importance. Twenty-three patients were recorded as Caucasians and 3 as negroes. The 3 negroes had primary operable gelatinous carcinomata.

### HISTORY OF LACTATION

No definite conclusions can be drawn from our study of the influence of lactation on the genesis of gelatinous carcinomata of the breast. Data concerning lactation were available in 20 patients, 12 of whom had nursed one or more children. Four of the eight cancers occurring in breasts which had never lactated, were in single women.

### TRAUMA

Seven patients gave a definite history of trauma to the afflicted breast while 6 others asserted that they could recall no injury. The character of the trauma varied. One patient had sustained injuries to the breast 48 years and again 4 years prior to the detection of the tumor. The average time elapsing between the trauma and the recognition of the cancer was 1½ years. No etiological importance can be ascribed to the history of trauma given by these patients, for two reasons; the interval of time was usually too great and the presence of pre-existing tumors could not be ruled out in the three instances in which the tumors appeared suddenly after injury. In our experience a single trauma has never caused cancer of the breast. We have no reason to believe that injury to an existent breast cancer can induce gelatinous degeneration.

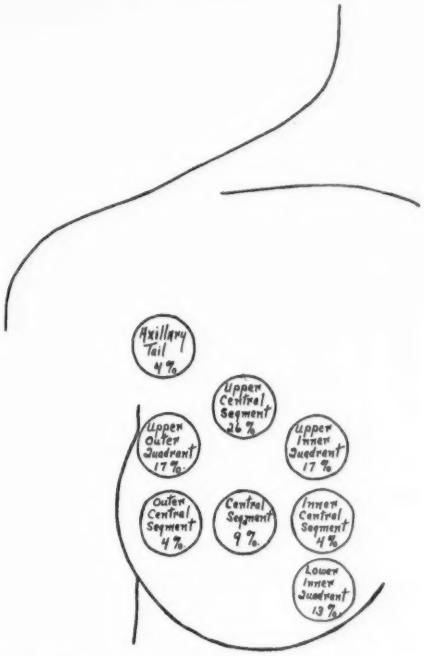


Fig. 14. Regional distribution of gelatinous carcinomata in the breast. The entire breast was involved in 1 case. The actual location of the tumor was recorded in 23 cases.

### CLINICAL SIGNS

*Halstead's sign.* Halstead described 5 cases of gelatinous carcinoma of the breast in which a "surprising swish" was detected (unintentionally) on palpation of the tumor mass. The diagnosis was correctly made in advance on the fourth and fifth cases on the basis of this sign which was detected in previous cases. It is "a peculiar sensation imparted to the examining fingers when examining the gland, as if something in the gland had suddenly burst, or ruptured, resulting in a sudden forcing of fluid out into the intercellular spaces."

As we have stated in the classification of gelatinous carcinomata of the breast, the tumor may appear as a localized, elastic, en-

Fig. 15. Axillary lymph nodes in gelatinous carcinoma of the breast. *A*, Node completely replaced by gelatin; *B*, node completely replaced by solid cellular metastatic carcinoma; *C*, node containing both gelatin débris and degenerating carcinomatous nests.

capsulated, movable mass exhibiting none of the characteristic features of malignancy or the gelatinous degeneration may develop in a pre-existent tumor modifying its course (Figs. 16 and 17). In the latter case, the patient frequently relates that a slow-growing, firm lump in her breast suddenly acquires an increased rate of growth and then becomes soft and fluctuant. Not all fluctuant carcinomata of the breast are of gelatinous character. The intracystic papillary cystadenocarcinomata and bulky adenocarcinomata with ischæmic necrosis and cavitation may be fluctuant but the possibility of a gelatinous carcinoma must be entertained when fluctuation is elicited in an obvious cancer of the breast. We have found an analogous course and history in a series of giant intracanalicular adenomyxomata of the breast (cystosarcoma phyllodes) in which the onset of gelatinous connective tissue changes in a long existent fibro-adenoma produces a rapidly growing, large, fluctuant tumor. In these giant adenomyxomata, the connective tissue of the benign fibro-adenoma becomes myxomatous and the tumor usually maintains its benignancy.

Carcinomata of the breast are usually opaque to transillumination, but if the gelatinous degeneration is great enough, this variety of mammary cancer may be translucent. Exploratory puncture and biopsy by means of an 18 gauge aspirating needle should be done and may demonstrate the gelatinous character of the tumor.

*First sign.* The histories of 24 patients contained a definite statement concerning the first symptom observed by the patient. Twenty-two patients (73 per cent) gave the discovery of a lump in the breast as their first symptom, and this finding parallels our experience in the survey of the first symptoms in one thousand cases of mammary carcinoma in general. Six of these patients had inoperable cancers at the time of diagnosis. A history of discharge from the nipple was obtained in none of the cases as compared with 1.5 per cent in the previously mentioned survey. Bleeding from the nipple was noted as the initial symptom in 4 case reports obtained from other sources; this sign would be expected as some of the gelatinous carcinoma arise in intraductal papillary carcinomata.

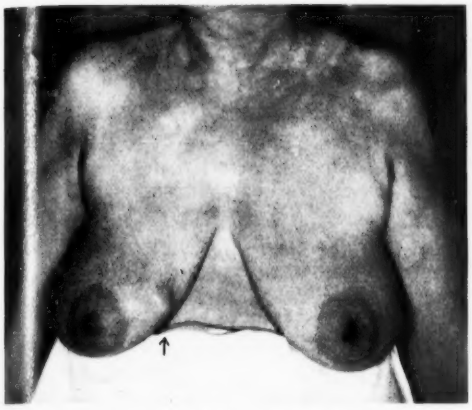

Fig. 16. An encapsulated, fluctuant, subcutaneous gelatinous carcinoma of the breast.

Fig. 17. A bulky encapsulated gelatinous carcinoma of the breast of slow growth rate, occurring in an elderly patient.

The first evidence of disease in 2 patients was pain in the breast, in the first, pain preceded the lump by 4 months, and in the second, it called the patient's attention to the mass in the breast. These 2 patients represent 6.6 per cent with pain as the first symptom as compared with 8 per cent in the one thousand breast cancers surveyed, which included all types.

### SIZE OF TUMOR

The size of the tumor was recorded in 14 cases of the primary operable and in 6 cases of the primary inoperable gelatinous carcinomata of the breast. Of the former group, 6 were greater than 6 centimeters, 6 were 3 to 6 centimeters, and 2 were less than 3 centimeters in diameter. In the latter group 4 were greater than 6 centimeters and 2 measured 5 centimeters in diameter. The largest tumor was found in the primary inoperable group measuring 15 by 15 centimeters and the smallest was in the primary operable group measuring 2 centimeters in diameter. The breast may be amputated while the tumor is small, but in the average case, the large size of the gelatinous carcinoma seems to be characteristic. Only 2 other varieties of mammary cancer are consistently as large, namely, the diffuse duct carcinomata and the bulky adenocarcinomata. Numerous case reports recorded in the literature verify this observation; the tumors are reported as large as a "cannon ball" or "fetal head," or weighing 3 to 7 pounds (Lebert, Demarquay, Robert, Larrey). Gaabe noted the size of the tumor in 60 reported cases; 6 were as large as a child's head, 13 were the size of a man's fist, and 50 per cent were the size of an apple. Ewing stated that mucoid carcinomata of the breast attain the largest dimensions of any mammary cancers. The clinical and pathological data contained in this article are one of the sources from which Ewing derived this conclusion. Cheatle and Cutler attribute the frequent large size of these tumors to an involvement of the entire duct system by the gelatinous neoplasia.

### LOCATION

Gelatinous carcinomata have no specific location in the segments of the breast. Dependable data concerning the location of the tumor were available for 23 cases of this series. Five of the 28 cases were recorded only as to the side (right or left) on which they were located. The accompanying diagram (Fig. 14) shows the regional tumor sites in these patients. The distribution was the same in the right and left breasts.

### PAIN

In gelatinous carcinoma of the breast, the unusual number of patients complaining of pain may be attributed to a sudden impetus in the rate of growth of the tumor often coincident with the gelatinous change. Sensory

disturbances varying from discomfort to severe lancinating pains in the breast often radiating down the arm or to the side of the chest were noted in 10 patients (33⅓ per cent). Nine of these patients experienced pain before treatment was given, 7 being in the primary operable group and 2 in the primary inoperable group. In the general group of breast cancers studied at the Memorial Hospital, pain has never been a frequent symptom, occurring in only 8 per cent of primary operable cancers.

### SKIN ADHERENCE AND NIPPLE RETRACTION

Twelve (66 per cent) of the primary operable gelatinous carcinomata of the breast were adherent to skin. These tumors were not in the purely gelatinous group. The nipple was retracted or fixed in only 24 per cent of all the cases due presumably to the fact that so many of these tumors were situated at the margins of the breast where they could not exert traction on the nipple. The localized, encapsulated, gelatinous carcinomata are not adherent to skin as they produce no desmoplastic changes in their neighborhood; this absence of skin dimpling and nipple retraction adds to the difficulty in the diagnosis of the benignancy or malignancy of these neoplasms. The gelatinous carcinoma ulcerates occasionally through the skin and discharges a glairy, greenish, mucinous slough. Three patients (42 per cent) of the primary inoperable group had fixed, immobile tumors.

### METASTASES

The frequency, rapidity, and regional limitation of metastasis in gelatinous carcinoma of the breast agree with our classification of these tumors into 2 groups. In the groups of ordinary mammary cancers undergoing gelatinous degeneration, the metastases follow the trend of the most malignant portion of the tumor. One patient with an anaplastic carcinoma of the breast in which some gelatinous changes were found died of generalized carcinomatosis. In general, however, metastasis is not so frequent in gelatinous carcinoma of the breast and these metastases appear late in the course of the disease. Gaabe computed the average period before dissemination in these carcinomata to be 40 months, as compared with 13 months for ordinary mammary cancers. The metastases from gelatinous carcinomata of the breast are further characterized by their relatively limited distribution, usually only to axillary lymph nodes, seldom to bones, lungs, and liver (Monod, Jayle). The metastatic lesions are not necessarily gelatinous.

*Metastasis to lymph nodes.* The axillary lymph nodes remain free of metastases for a long time (Binaud and Braquehaye) and when involved the process is relatively inactive so that the duration of operability is longer than obtained for other mammary cancers. Gaabe estimated that the interval before involvement of the axillary lymph nodes is three times as long as for ordinary carcinomata of the breast. The axillary lymph nodes may contain solid carcinoma or a trace of gelatinous metamorphosis; in other cases, the lymph nodes are entirely replaced by transparent gelatinous carcinoma (Fig. 15). Ten of our patients (55 per cent) with primary operable gelatinous cancers had metastases in the axillary lymph nodes; 7 of these were verified histologically. The primary tumor in 70 per cent of these cases involved the upper outer quadrant of the breast of the axillary tail. Five patients (71 per cent) with primary inoperable gelatinous cancers had axillary metastases; 1 had supraclavicular involvement. Only 1 of the patients (25 per cent) with recurrent gelatinous cancer of the breast had metastasis in the axillary and supraclavicular nodes. The number of cases is too small to compare with the ordinary recurrent carcinomata of the breast, which we have found to be accompanied by metastasis in the axillary lymph nodes in 60 per cent of cases.

*Metastasis to lungs and pleura.* Gelatinous carcinomata of the breast are said to involve the lungs and pleura twice as frequently as the liver and abdominal lymph nodes (Gaabe, Lebert). One patient in the primary operable group developed pulmonary metastases 8 months after a radical mastectomy. Two patients (28 per cent) of the primary inoperable group had pulmonary metastases demonstrable in the roentgenograms.

*Metastasis to bone.* Only 2 patients (6 per cent) of the entire series presented definite evidence of metastasis to bone. One young woman of 40 years developed rib metastases 5 months after a radical mastectomy. High voltage roentgen therapy was administered to the involved bones. This patient is still living and well 2½ years after the operation. The other patient developed metastases to the skull 5 months following a radical mastectomy and metastases to the pelvis, spine, and femurs 3 years after operation. Both preoperative and postoperative irradiation had been given. Death from generalized carcinomatosis took place in 3 years and 11 months after treatment was instituted.

### END-RESULTS

Of the 18 patients with gelatinous carcinoma of the breast, classified as "primary operable," 3 are dead, 11 are living, and 4 have been lost to our observation. One of these latter 4 patients was known to have been free of carcinoma for 3 years after treatment. The length of life from the onset of symptoms to death in the 3 patients who died was 6, 5½, and 2 years, an average of 4½ years. The average length of life of patients in these fatal cases after the institution of treatment was 3 years. Seven of the patients having primary operable gelatinous cancers of the breast were treated prior to July, 1928. In this group 1 has been lost to further observation and 4 (57 per cent) are alive and well 5 years or more after treatment. Two of these patients (28 per cent) were treated prior to July, 1926, and both are living and well 7 years after treatment. The percentage figures of the 5 year survivals are higher than the end-result percentages recently computed at the Memorial Hospital for primary operable mammary cancers of all histological types; viz., 5 year survival without evidence of disease in 217 patients treated by radical mastectomy with irradiation before and after operation, 41 per cent. In the 7 year survival group the latter statistics revealed 35 per cent. With so few cases in the group under present consideration, it is difficult to conclude that the degree of malignancy and the prognosis following treatment are the same as for the general group of mammary cancers. If a large groud of gelatinous carcinomata of the breast could be surveyed with respect to end-results, the comparison would be more significant.

In the primary inoperable group consisting of 7 patients, 4 are dead and 3 are living. The cause of death in 1 patient was cerebral hæmorrhage at the age of 89, 15 years after the onset of the disease and 6 years after the local mastectomy. The average duration of life after the onset of symptoms was 4.8 years. The average duration of life after the initiation of therapy in these inoperable cases was 3.7 years, the longest being 10 years and the shortest 6 months. Our 3 patients who are now alive were first treated 11 years, 2½ years, and 2 years ago. The one who has lived 11 years without recurrence was 55 years old when first seen in November, 1922. She had a movable tumor, 5 centimeters in diameter, in the upper inner quadrant of the right breast with skin adherence, axillary and supraclavicular metastases. She was treated with bare radon seeds, radium emanation pack, low voltage X-ray cycle, local mastectomy, and postoperative low voltage X-ray cycle.

CASE 2. Primary inoperable gelatinous carcinoma of the breast.

E. F., a white married woman, 55 years of age, was first seen at the Memorial Hospital on July 10, 1922, because of a lump in her right breast. She had been struck on the right arm and breast with a black-jack 1 year prior to her application. A movable tumor, adherent to skin and measuring 5 centimeters in diameter was found in the upper central segment of the right breast. A firm, enlarged, lymph node was palpated in the right axilla. The carcinoma was classified as inoperable because of fullness of the right supraclavicular space. A biopsy was reported by Dr. Ewing as gelatinous carcinoma of the breast.

In the course of the next year, two pre-operative low voltage X-ray cycles were given to the right breast and drainage areas, followed by the implantation of glass filtered radon seeds, 9 seeds containing 15 millicuries and 14 seeds containing 17 millicuries with an interval of 3 months. Following this a local mastectomy was performed and at the same time 9 glass radon seeds containing 8 millicuries were inserted in the right axilla. The right supraclavicular space received two additional low voltage X-ray treatments and two exposures to the radon pack (9,000 millicurie hours) with a filter of 2 millimeters of brass and a radium skin distance of 6 centimeters. There was no evidence of carci-

noma at the time of the last observation, June 6, 1933, 11 years after treatment.

There were 4 patients who had recurrent gelatinous carcinomata of the breast. All are living and well. One patient had a recurrent nodule in a scar, 25 years after a radical mastectomy had been performed in another institution. The treatment in February, 1927, consisted in the excision of the nodule and the application of a radon tray for 3,000 millicurie hours. The patient was last seen on July 11, 1933, at which time no evidence of carcinoma was present. The average duration of life of these 4 patients from the onset of the recurrence to the time of the last observation was 3 years. The time elapsing between the operative treatment of the primary tumor and application at Memorial Hospital because of recurrence, averaged 18 months for 3 patients, the fourth being 25 years. The shortest period in which recurrence developed was 5 weeks.

TABLE III.—SUMMARY OF CASES

| | Living | Lost to observation | Dead |
|---|---|---|---|
| Primary operable | 11 | 4 | 3 |
| Primary inoperable | 3 | · | 4 |
| Recurrent | 4 | · | · |
| Total | 18 | 4 | 7 |

## SUMMARY

1. Gelatinous carcinomata occur in many organs of the body which normally secrete mucus. A rare and interesting type of gelatinous carcinoma is that occurring in the breast.

2. The incidence of this type of carcinoma ranges between 1 and 2 per cent of all breast cancers.

3. Gelatinous carcinoma of the breast occurs in two main forms; (a) primary gelatinous carcinoma in which the gelatinous features predominate; (b) ordinary carcinoma of the breast with secondary gelatinous degeneration. The latter type may be divided into the myxoid or mucoid carcinoma depending on whether the gelatinous changes arise by metaplasia in the connective tissue or by secretion directly from the carcinoma cells respectively.

4. In the majority of cases the epithelial cells of the tumor are the source of the gelatinous material by a secretory process. Less frequently the connective tissue assumes myxoid characteristics by a degenerative process.

5. Gelatinous carcinoma of the breast is usually slower in growth than the ordinary carcinoma. One of the reasons given for this fact is that the tumor arises on the basis of a pre-existing benign mammary adenoma in many instances.

6. No essential differences are observed in age, sex, and race distribution, history of lactation, and of trauma between the gelatinous carcinomata and ordinary mammary carcinomata.

7. The diagnosis of gelatinous carcinoma of the breast is made on the slow growth of the tumor, Halstead's sign, the usual signs and symptoms of ordinary breast carcinoma, and on the aspiration or punch biopsy.

8. Metastases from gelatinous carcinoma of the breast occur late in the course of the disease as compared with the usual type of mammary carcinoma, are usually confined to the axillary lymph nodes, and do not necessarily show gelatinous changes.

9. The end-results of our 30 cases of gelatinous carcinoma of the breast indicate a considerably higher percentage of cures than in the usual types of carcinoma of the breast. The degree of malignancy is lower than in other carcinomata of the breast as evidenced by 57 per cent of 5 year cures as compared with 41 per cent in a control group.

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# THE RELATION OF RECOVERY OF DIFFERENT SENSORY BRANCHES OF PERIPHERAL NERVES TO MOTOR RECOVERY[1]

LEWIS J. POLLOCK, M.D., CHICAGO

IN a contribution (2) on the rôle of overlap in early return of some forms of sensation, I stated: "I have never found a return of sensibility to pain when sensibility to touch has not returned, except in an area of overlap." Foerster (1) believed this to be incorrect in the majority of instances. This seeming difference of opinion arises, I believe, in my failure properly to define my meaning. The observation was described in an article dealing with the early return of sensibility, *not* the result of regeneration. The material for this study, therefore, dealt with severe injuries, mostly confirmed at operation to be complete anatomical sections. No regeneration was present. Despite the anatomical section, protopathic sensation had returned in an area lying within the border of the sensory supply of the several nerves. What I meant to say was that whenever return of sensibility had been shown to be the result of overlap and not of regeneration, I had never found a return of sensibility to pain when sensibility to touch had not returned, except in an area which was found by a study of residual sensibility to be one of overlap. It is well known, and has likewise been observed and described by me (3), that when sensation returns as the result of regeneration, sensibility to pain alone may return within the area of the isolated supply of a nerve, or touch or temperature senses alone recover in such an area.

My interest being aroused by this difference of opinion, I had occasion to review some of my sensory charts. It occurred to me that one might find some correlation between the recovery of some individual sensory branches of a nerve and the return of motor function in muscles, the nerves to which were given off at levels corresponding to the sensory ones. For example, was the return of sensibility in the internal plantar nerves correlated with the return of function in any particular muscles in the foot?

Sensory charts of recovering ulnar, median, radial, peroneal, and sciatic nerves were studied. Certain muscles supplied by these nerves were charted in terms of recovery, complete or expressed in dynamometric pounds, or paralyzed, and the areas supplied by individual sensory nerves plotted against them in terms of recovery (R), partial recovery (hatching), overlap (o), and complete loss of sensation (black).

## ULNAR NERVE—FIGURE 1

The dorsal cutaneous branch of the ulnar nerve may be given off above the elbow, although it is usually given off in the middle one-third of the forearm. It supplies the dorsum of the little and ulnar half of the ring fingers and the corresponding part of the dorsum of the hand. Variations occur but this is the usual supply.

The palmar branch arises in the lower third of the forearm. It supplies the palm. The ulnar nerve divides in the palm into the superficial and deep. The latter is purely motor; the former ends by dividing into the inner and outer digital branches; the former supplies the inner side of the little finger, the latter the adjacent sides of little and ring fingers.

In 26 cases of injury above the middle third of the forearm, operation had been done in 10, indicating severe lesions. Of these, 4 showed no return of sensibility, 4 return of sensibility as the result of regeneration, and 2 only of overlap. In the 16 remaining there was 1 with complete recovery in sensation and in this case there was no return of motion (a notable exception); 8 cases with return of sensation as the result of regeneration, 4 of complete loss of sensation, and 3 of overlap. Recovery was seen in the digital branches when none had occurred in the dorsal cutaneous, but when some recovery had occurred in the latter, sensation was always found to be recovering in the digital branches.

[1] From the Department of Nervous and Mental Diseases of Northwestern University Medical School.

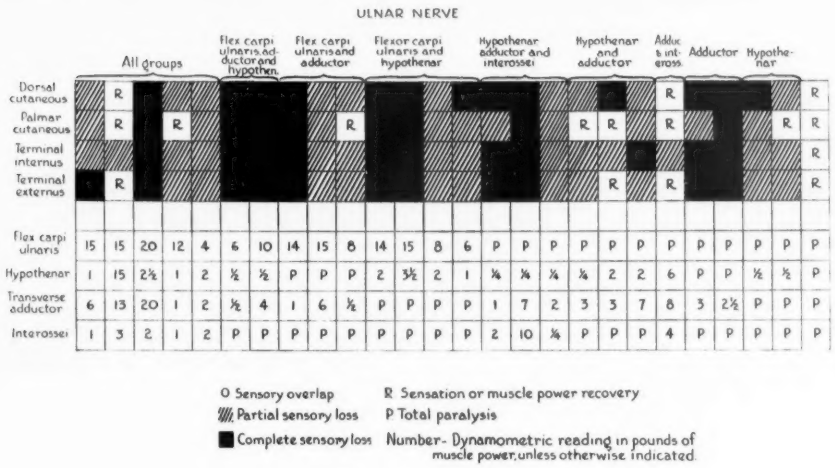


Fig. 1. Ulnar nerve.

The return of motor power in the hypothenar muscles or in the adductor of the thumb had no relation to any possible sensory recovery in any special branches, as the digital, palmar, or dorsal cutaneous. Neither did the return of function in the flexor carpi ulnaris have any correlation with particular sensory regeneration. Of all 26 cases showing some motor recovery, sensory regeneration was observed in 13 cases, or 50 per cent. In the cases in which operation was done 40 per cent were recovering and in those not operated upon 56 per cent.

### MEDIAN NERVE—FIGURE 2

The palmar cutaneous branch arises in the lower third of the forearm and supplies the skin of the palm. The digital cutaneous branches, which are the terminal branches in the hand, are five in number; the first and second, supply each side of the thumb; the third, the radial side of the index finger; the fourth, the adjacent sides of the index and middle fingers; and the fifth, the adjacent sides of the middle and ring fingers.

In 19 cases of median nerve injury above the middle third of the forearm, there were 12 with return of sensibility due to regeneration and in 7 the return of sensibility could be attributed to overlap. In all there was some return of sensibility. In 12 cases in which recovery was observed in the cutaneous digital nerves, 8 also showed recovery in the palmar branch, 3 only overlap, and in 1 there was no recovery. In this particular case the palmaris longus and the flexors of the fingers and the flexor of the thumb were recovering.

There was no relation between the recovery of particular muscles and the return of sensation in any particular cutaneous nerve.

In 15 of 17 cases of recovering ulnar and median nerve lesions sensory loss of the median was incomplete. In only 4 of the 17 was the sensory loss of the ulnar incomplete. In only 2 cases was there sensory loss of the median when motor regeneration was evident.

### RADIAL NERVE—FIGURE 3

The internal cutaneous branch distributed to the skin of the arm behind the area supplied by the intercostohumeral nerve is given off in the upper part of the arm. The superior external cutaneous, supplying the lower half of the back of the arm and back of the elbow, and the inferior, supplying the back of the arm in its lower third and the back of the forearm in its upper two-thirds, are given off in the middle of the arm. The radial nerve distributed to the back of the lower one-third of the forearm and the back of the hand and fingers is given off at about the elbow. It supplies the whole dorsum of the thumb,

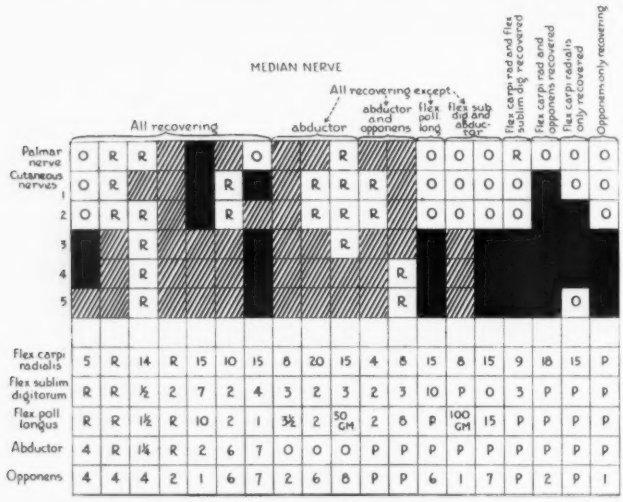


Fig. 2. Median nerve.

the skin on the proximal phalanx of the forefinger and part of the proximal phalanx of the middle finger, and at times the skin between the proximal phalanges of the middle and ring fingers.

Of 38 cases of injury to the radial nerve 12 had been operated upon. In these the sensory loss of the radial nerve was more extensive than in the 26 other cases in which no operation was done. In 6 cases of complete motor paralysis there was sensory return as the result of regeneration in 2 and only overlap in the rest. Where in 5 cases the extensor carpi radialis alone had recovered there was sensory regeneration in 1 case; when in addition, the extensor carpi ulnaris recovered in 2 cases, in 1 there was sensory regeneration; when in addition to the extensor carpi radialis there was recovery in the extensor longus pollicis or the common extensor, sensory recovery was shown in 2 cases; when in addition to the extensor carpi radialis, 2 other muscles also were recovering, there was recovery in the sensation in all of the 4 cases. In 5 cases of recovery of the extensor longus pollicis alone, there was sensory recovery in 4 of the 5 cases, and in 6 cases in which motor recovery was occurring in all muscles, there were 3 cases with complete sensory regeneration and 3 with recovering sensation. Of the 38 cases, there were 7 cases with complete sensory recovery, 6 with complete sensory loss, 5 with overlap, and the remaining 20, recovering sensation.

In addition to the observation that there was more sensory recovery the more motor return was noted, it is notable that return of function of the extensor longus pollicis and the extensor communis digitorum are related to sensory recovery. In 16 cases in which the extensor longus pollicis was recovering there was sensory regeneration in 14, and in 10 cases in which the extensor communis digitorum was recovering all showed sensation to be recovering; whereas in 13 cases in which there was no recovery in the extensor longus pollicis or extensor communis digitorum in only 4 cases was sensory regeneration noted. When recovery was noted in the cutaneous branches there was also recovery in the radial supply.

### PERONEAL NERVE—FIGURE 4

The sural branches to the skin over the back and outer side of the calf are given off in the popliteal space and may be spared when all the muscular branches of the peroneal are paralyzed. The musculocutaneous to the front of the leg and the dorsum of the foot and toes arises in the upper third of the

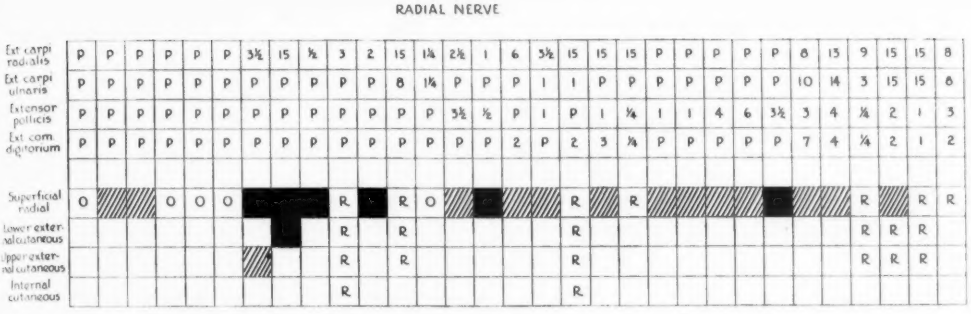


Fig. 3. Radial nerve.

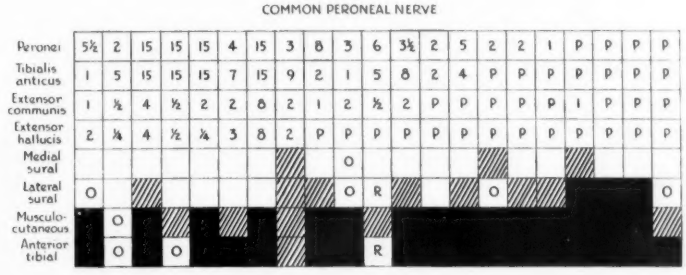


Fig. 4. Common peroneal nerve.

leg; below the middle third of the leg it is purely sensory. The internal terminal branch of the anterior tibial, which is given off in the popliteal space, supplies the adjacent side of the first and second toes and a small area of the dorsum of the foot.

In 21 cases of peroneal nerves injured above the upper third of the leg, there was evidence of some motor recovery in all of the muscles supplied by this nerve in 8 cases. Of these there was evidence of sensory regeneration in 4. In 4 other cases where the extensor pollicis had not recovered there was sensory regeneration in 3. In 2 cases in which the extensor communis digitorum and extensor hallucis were not recovering there was sensory regeneration in 1. Where in 3 cases only the peronei were recovering there was sensory regeneration in all and when all the muscles were paralyzed sensory regeneration occurred in 1 case, as it did in a case of recovery only of the extensor communis digitorum. However, when we analyze this sensory recovery we find in the first group recovery not only in the sural branches but in the musculocutaneous and anterior tibial as well. In the second group, whereas recovery in the sural branches occurred in 3 cases, recovery in the musculocutaneous and anterior tibial occurred only in 1 case. In the third group in which some sensory regeneration was observed in 1 case it was confined to the sural branch. In the fourth group the sensory regeneration occurred only in the sural nerves, and in the fifth and sixth groups sensory regeneration in the musculocutaneous or anterior tibial occurred only once. There was recovery in the musculocutaneous or anterior tibial in only 5 of 19 recovering cases. In this series in which sensory loss had been observed in the sural branches soon after injury it was noted, and in the cases which on the chart have no notation, no sensory loss had been present in the sural branches. It may be said, therefore, that in general with less muscular recovery there is less recovery in the sural branches. But in many cases the peroneal nerve is injured before the sural branches are given off

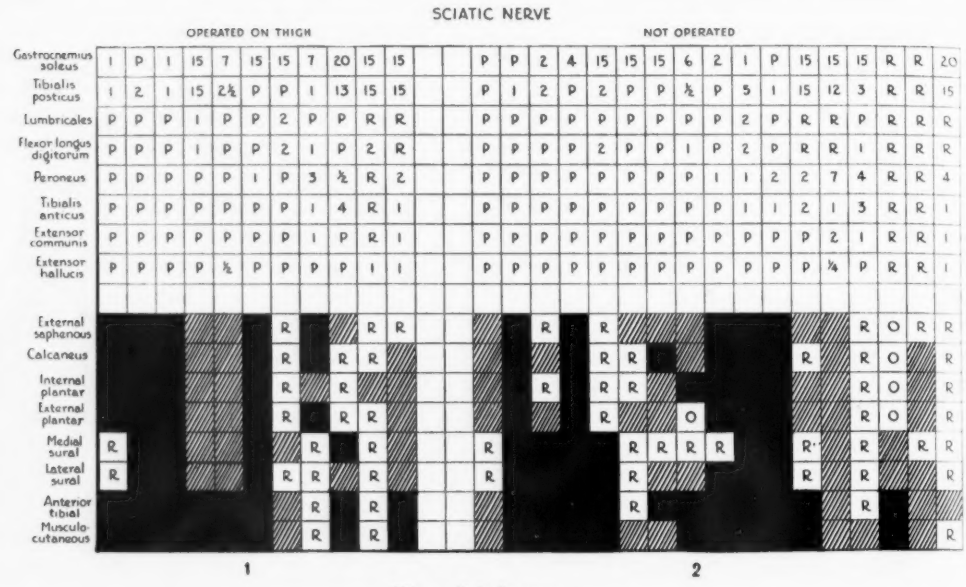


Fig. 5. Sciatic nerve.

and we are then dependent upon a study of the musculocutaneous and anterior tibial nerves. We note that with recovery in all the muscles sensory recovery of these nerves occurred in only 3 of 8 cases, and of the 13 remaining cases in only 2. In this regard the peroneal nerve resembles more the ulnar nerve, not, as might be expected, the radial nerve, in which there is a definite correlation between sensory regeneration and motor recovery.

In the peroneal nerve it may also be said that there is no correlation between individual sensory nerve recovery and particular muscle regeneration, except that more cases showed sensory recovery in the musculocutaneous and anterior tibial where some recovery occurred in the extensor hallucis and communis digitorum muscles.

### SCIATIC NERVE—FIGURE 5

The sensory supply of the peroneal nerve has already been described.

The external saphenous nerve supplies the distal part of the lower third of the leg on the outer side and the outer side of the foot and little toe. It may supply the skin of one and a half toes on the outer side of the foot and rarely spread on to the dorsum of the foot. It is formed by the communicans tibialis arising in the popliteal space and the communicans fibularis from the peroneal. In such cases, in which there is failure of union, the tibial branch supplies the foot, the fibular the leg. The nerve is given off above all of the motor branches to the foot and toes.

The calcanean nerve arises from the posterior tibial in the lower third of the leg and supplies the skin of the heel and the back part of the sole.

Below the internal malleolus the posterior tibial divides into the internal and external plantars. The internal supplies sensation to the inner part of the sole to a line dividing the next to the little toe, the flexor brevis digitorum, adductor hallucis, the flexor brevis hallucis, and the first lumbrical muscles. The external plantar supplies the inner one and a half toes and corresponding part of the sole with sensation and the rest of the small muscles of the foot.

The 46 cases of injury to the sciatic nerve may be analyzed in six groups:

1. Injured above the knee, 11 cases, operated upon.

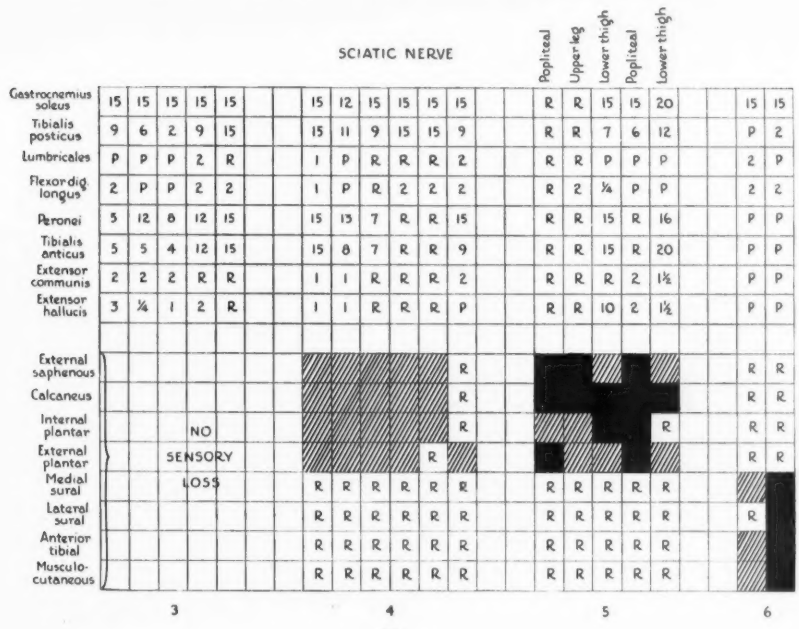


Fig. 5.

2. Injured above the knee with one exception showing sensory loss in peroneal or tibial nerves, 17 cases, not operated upon.

3. No sensory loss, 5 cases, not operated upon.

4. No sensory loss in the peroneal, 6 cases, not operated upon.

5. Injured in the lower part of the thigh or popliteal space with recovery in the sensory function of the peroneal nerve, 5 cases, not operated upon.

6. Injured in the thigh with sensory recovery in the tibial nerve, 2 cases, not operated upon.

In the first group of cases in which operation was carried out, when motor recovery has occurred only in the tibial nerve, sensory recovery in the peroneal was limited to the sural branches. Of 8 cases showing sensory recovery in the peroneal nerve only 3 showed recovery in the musculocutaneous and anterior tibial, similar to the lesions of peroneal nerve alone. This occurred, however, in the cases showing greater motor recovery. In 6 of the 11 cases, all of which showed varying degrees of motor recovery in the tibial, there was sensory recovery.

With the one exception when some sensory regeneration occurred in the peroneal it was also found in the tibial.

In the second group of 17 cases not operated upon, in 8 cases in which there was no motor recovery in the peroneal, there was sensory recovery in 4 and in 3 of these it was found in the musculocutaneous or anterior tibials. When one or two muscles supplied by the peroneal had recovered, there was sensory regeneration in 2 and these only in the sural branches. When 3 or more muscles had recovered, of 5 cases, there was sensory regeneration in 4 including the musculocutaneous and anterior tibial, so that in sciatic nerve lesions sensory recovery occurs more frequently in these nerves than in lesions of the peroneal nerve. In 9 cases showing recovery in the musculocutaneous and anterior tibial, motor recovery was noted in the extensor hallucis or communis digitorum in 6, although sensory return was seen in 3 when these muscles were paralyzed. Of the combined first and second

groups, in 10 of 28 cases, there was sensory regeneration. In cases in which complete motor paralysis of the tibial nerve may be present, marked sensory regeneration may be found and in cases in which complete recovery had taken place no sensory regeneration may be found. However, when motor regeneration was more complete in the tibial, sensory regeneration was found to be further advanced.

In 27 cases in which some motor recovery had taken place in the tibial nerve, 18 cases showed some sensory recovery. Return of sensation in the external saphenous seemed to show some relation to recovery of the gastrocnemius.

In group 3 there was no sensory loss in either tibial or peroneal, despite the incomplete motor recovery which, however, was fairly well advanced.

In group 4, sensory regeneration may be progressing in the tibial nerve and no sensory loss found in the peroneal nerve, when motor regeneration had progressed to a marked degree in both nerves.

In group 5, despite the marked motor regeneration in the tibial and peroneal nerves, there was more severe sensory loss in the tibials, although some regeneration was seen in all of them but one. In the peroneal nerve, sensory recovery was found to be complete.

In the last 3 groups it is obvious that in the first the sensory nerves of both divisions of the sciatic nerve sustained a lesser injury and in the last 2 the peroneal sustained a lesser injury. In the last group the tibial nerve showed some motor recovery and complete sensory recovery and the sensory branches were probably injured to a lesser degree. This more complete recovery in tibial or peroneal or both nerves supports Stoeffel's intraneural localization, at least so far as the existence of separate bundles at a certain level for sensory nerves is concerned. This observation has been noted by many and adequately discussed by Foerster. Parenthetically it may be said that Foerster's observation of the larger area of the loss of temperature sense, as compared to tactile sense, was confirmed by this study.

## CONCLUSIONS

1. One hundred sixty-seven records of sensory regeneration in recovering nerves have been analyzed to determine any possible relation between the motor recovery of certain muscles innervated by injured nerves and sensory regeneration, in particular sensory cutaneous branches.

2. Sensory regeneration did not appear to be co-extensive with motor recovery of the ulnar nerve, occurring in only 50 per cent of cases. There was no specific relation between return of sensation in individual nerves and motor recovery of certain muscles.

3. When motor function was returning in injuries of the median nerve, sensory regeneration could be demonstrated in 63 per cent of cases and overlap in the rest. No relation could be found between sensory return and recovery of individual muscles.

4. In most of the cases of injury of both ulnar and median nerves, sensory loss in the median was incomplete in about 88 per cent of cases, while only 23 per cent of ulnar nerves showed incomplete sensory loss.

5. Eighty per cent of recovering radial nerves showed sensory regeneration; a greater proportion of cases in which regeneration was found in the extensor longus pollicis and extensor communis digitorum showed sensory regeneration than when the extensors of the wrist were recovering.

6. The more muscles recovering in peroneal nerve lesions, the more numbers of cases showed sensory regeneration of the sural nerves. The musculocutaneous and anterior tibial nerves showed sensory regeneration in only 26 per cent of all cases, thus corresponding to the ulnar nerve. No correlation could be found between sensory and motor recovery.

7. In injuries of the sciatic nerve motor recovery in the peroneal nerve is associated more frequently with sensory regeneration in the musculocutaneous and anterior tibial nerves than in isolated lesions of the peroneal nerve, and sensory regeneration is related somewhat to motor recovery in the extensor communis digitorum and extensor hallucis.

In some cases in which the tibial nerve was completely paralyzed, marked sensory regeneration was found, and in other cases in which

complete motor recovery was present, no recovery of sensation was found.

Complete recovery of sensation in tibial and peroneal nerves was found in cases with partial motor recovery. Complete sensory recovery of either the tibial or peroneal nerve was found when motor recovery was incomplete, showing a gross intraneural localization.

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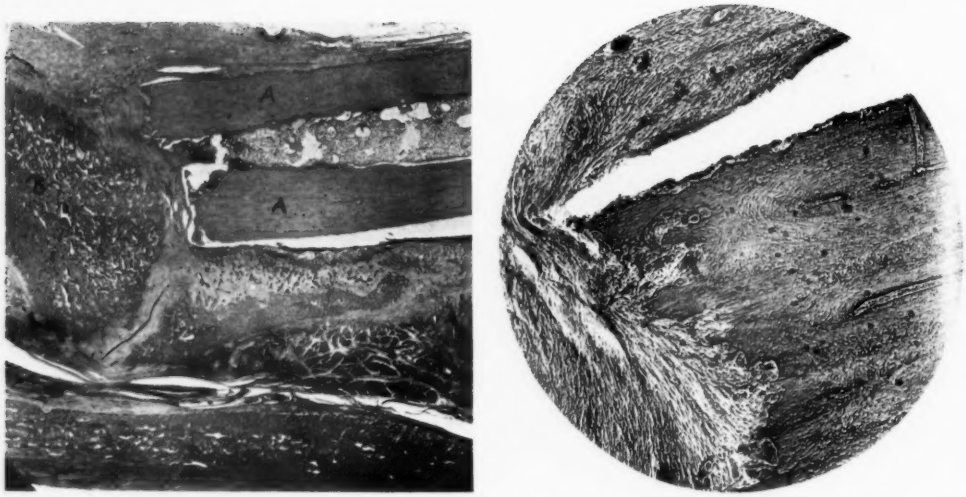


Fig. 1. Boiled segment, 30 days. Low power of dead graft, *A*, new bone growth from end of radius, *B;* higher power, in circle, shows surface absorption of the dead graft with no evidence of new bone growth.

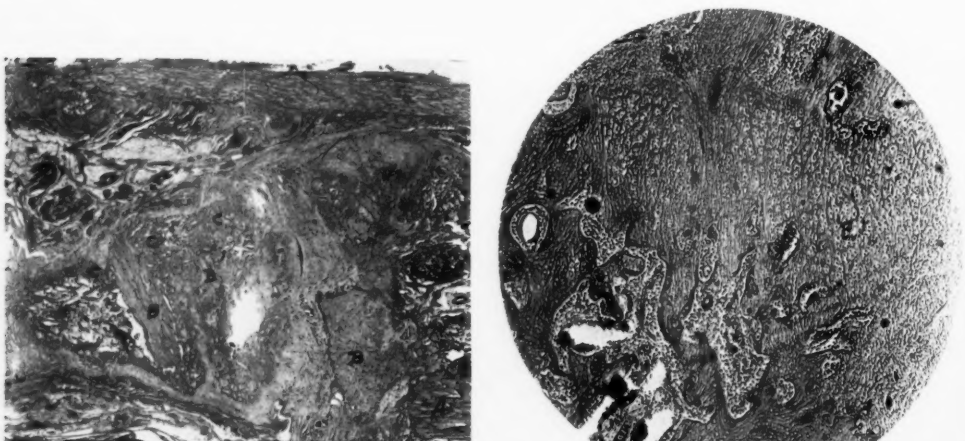


Fig. 2. Fragmented segment, 30 days. Low power showing end of radius, *A;* grafts, *B;* new bone growing from them, *C;* higher power circle showing a portion of a graft with empty lacunar spaces and some surface absorption, D, but with active new bone growth arising from it, *E*.

*Experimental Bone Regeneration.—William J. Stewart.*

# EXPERIMENTAL BONE REGENERATION

## Using Lime Salts and Autogenous Grafts as Sources of Available Calcium[1]

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ATTEMPTS to perfect a means of stimulating bone growth are of interest to the clinician and research worker alike. In recent years, the use of living bone grafts has become a standard procedure in treating non-union, performing fusion operations, and the like. Henderson has advocated the use of massive bone grafts in non-union and has demonstrated the effectiveness of this procedure. Phemister has obtained excellent results with splint grafts. The use of autogenous bone grafts, whether in the form of the massive graft, splint graft, osteoperiosteal graft, or simply bone chips, has become well established.

Numerous studies have been carried out with relation to calcium and phosphorous metabolism in an effort to stimulate bone growth. Circulatory alterations have been studied (5) for the same purpose. Naturally, the introduction of lime salts into the area where stimulation of bone growth is desired has been done, particularly by Murray.

Recently the exhibit (3) of Murray which was preserved at the headquarters of the American Medical Association in Chicago was inspected and a series of experiments carried out to attempt to verify his findings. Healthy dogs were chosen as the experimental animals. The composition of the lime salts which was introduced into the bone defects was $Ca_3(PO_4)_2$, 85 per cent and Ca $CO_3$, 15 per cent. Hastings and Zachariasen showed by X-ray spectrum analysis that these two salts are in combination because only tricalcic phosphate [$Ca_3(PO_4)_2$] lines show in X-ray spectrographs. The animals were operated upon under aseptic conditions. A small number of them became infected and were discarded but a reasonably large number of animals survived in good shape so that quite definite results were obtained.

The following procedures were carried out on healthy adult dogs:

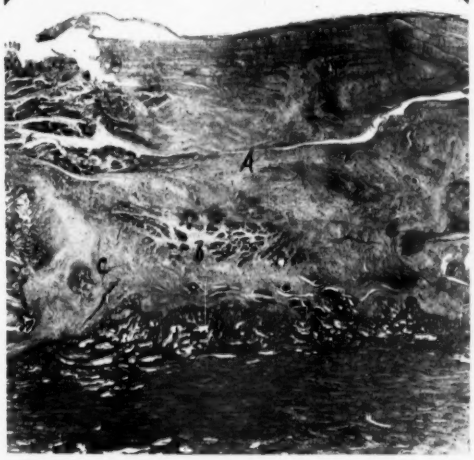


Fig. 3. Radial defect filled with lime salts, 30 days. Low power showing defect filled with fibrous tissue, *A;* muscle strands, *B;* an occasional bone chip left behind at operation, *C;* marked adjacent ulnar hypertrophy, *D.* No evidence of the salts or new bone growth due to them.

Fig. 4. Fascial bag filled with lime salts, implanted in the radial defect, 30 days. Defect filled with fibrous tissue with no evidence of new bone growth, *A;* beginning ulnar hypertrophy, *B.*

[1]This work was done under a grant of the Douglas Smith Foundation for Medical Research of the University of Chicago.

TABLE I.—SUMMARY

| Procedures | Necropsy findings | | Roentgen findings | | | Microscopic findings |
|---|---|---|---|---|---|---|
| | Days | Union | Callus formation | Other changes | Description | |
| 1. Excised radial segment. Boiled 10 minutes. Replaced | 30 | Fibrous | None | | Graft retains original density, with decreased density of adjacent radial ends. No bony union of graft to radius. Some new bone growth in defect, not associated with the graft, but arising from one end of the radius. Ulna fractured, healed, shows definite hypertrophy | Graft is dead. Shows moderate surface absorption. One end of the radius shows marked surface absorption, the other end shows a large amount of new bone formation. No new bone growth in relation to the graft. Ulna adjacent to the graft is hypertrophied (Fig. 1) |
| | 60 | Fibrous | None | | Graft retains original density, with some decreased density of adjacent radial ends. No union of graft to radius. Many small areas of calcification around the graft, apparently bone chips. Ulna has fractured, healed, and shows definite hypertrophy | Graft is dead and surrounded by a mass of fibrous tissue and new bone growth, which latter arises from the ends of the radius, not from the graft. Marked surface absorption of the graft with a few areas of creeping substitution. Medullary cavity of graft filled with fibrous marrow, with absorption of the trabeculæ, but no new bone growth |
| 2. Excised radial segment, fragmented and fragments replaced | 30 | Firm | Marked | | Fragmented grafts are *in situ*. Appear to be of same density as adjacent radius and ulna. Definite callus formation about them | Fragmented grafts are dead but are surrounded by a mass of new bone growth arising from them and the adjacent ends of the radius. Some areas of creeping substitution just beginning. The amount of new bone growth is in marked contrast to the preceding sections where the grafts were boiled and there was no new bone growth from them (Fig. 2) |
| | 60 | Firm | Bony, large amount | | Fragmented grafts have a more homogeneous uniform appearance than in the preceding specimen. Definite adjacent ulnar hypertrophy | Fragmented grafts are dead and are embedded in new bone growth arising from them and the adjacent cut ends of the radius. Process is simply more advanced than in the preceding section. Grafts are about 50% transformed by creeping substitution. |
| 3. Excised radial segment filled with salts | 30 | None | None | | No evidence of calcification or bone growth in the defect. *Non-union* | Active new bone growth from the ends of the radius. Defect is filled with a mass of fibrous tissue, a few muscle strands and an occasional bone chip showing active bone proliferation. No evidence of the implanted calcium salts or new bone growth resulting from them. Marked adjacent ulnar hypertrophy (Fig. 3) |
| | 60 | None | None | | No evidence of calcification or bone growth in the radial defect. Ends of the radius are rounded off, smooth, and show generalized decreased density. *Non-union* | Ends of radius show marked absorption and no new bone growth. Defect is filled with fibrous tissue and muscle strands, with no evidence of implanted calcium salts or new bone growth. Radial ends show definite pointing, characteristic of non-union |
| 4. Excised segment replaced by fascial bag containing salts | 30 | None | None | | Defect contains no evidence of calcification, new bone growth from radial ends, particularly the proximal one. *Non-union* | Ends of radius show definite new bone growth. Defect filled with fibrous and muscle tissue containing several small areas of calcification, as shown by deeper stains, and several small vacuoles from which calcium may have been absorbed. No new bone growth (Fig. 4) |
| | 60 | Infected | Discarded | | | |
| 5. Excised radial segment, replaced with salts and traumatized muscle | 22 | None | None | | Radial defect contains no evidence of calcification or bone growth. In adjacent soft tissue apparently between fascial planes there are many flecks of calcific material. Radial ends show no new bone growth but are smooth, rounded. *Non-union* | New bone growth from radial ends. A few bone chips surrounded by new bone growth. Defect is filled with fibrous and muscle tissue containing a few small areas of calcification but no new bone growth. (Fig. 5) |
| | 35 | None | None | | Radial defect contains a few flecks of calcific material, which are also seen out in soft tissues, extending to elbow joint. Radial ends smooth, pointed. *Non-union* | One radial end shows marked absorption, the other some new bone growth and a considerable amount of creeping substitution. Defect filled with fibrous and muscle tissue containing one area more deeply stained suggesting remaining calcium salts. No evidence of new bone growth |

TABLE I.—SUMMARY—Continued

| Procedures | Necropsy findings | | Roentgen findings | | | Microscopic findings |
|---|---|---|---|---|---|---|
| | Days | Union | Callus formation | Other changes | Description | |
| | 45 | None | None | | No evidence of calcification or new bone growth. Fragments smooth, rounded. Ulnar hypertrophy. *Non-union* | One radial end shows definite new bone growth, the other marked absorption and creeping substitution. Defect is filled with fibrous tissue and contains two small bone chips showing active proliferation and transformation. No evidence of implanted calcium salts or new bone growth due to its presence |
| | 60 | None | None | | No evidence of calcification or bone growth in the defect. Radial ends smooth, pointed. *Non-union* | Radial ends show marked absorption and pointing, no new bone growth. Defect contains fibrous tissue, with no evidence of implanted salts or new bone growth |
| 6. Excised radial segment with salts in gelatin capsule | 30 | Infected | Discarded | | | |
| | 60 | None | None | | Large area of calcification in operative defect, with rounding off of adjacent ends and ulnar hypertrophy. *Non-union* | Marked new bone growth from the radial ends, with areas of absorption and creeping substitution. Defect filled with fibrous tissue containing no evidence of implanted calcium salts or new bone growth |
| 7. Excised carpal bone replaced with salts | 30 | | | No evidence of new bone regeneration | Defect in carpal due to excision of bone. Non-evidence of calcification or bone growth. Cartilage spaces thin. *Arthritis* | Carpal bones are alive, covered with live cartilage which show occasional defect with invasion of cartilage and subchondral bone by fibrous tissue, evidence of arthritis. No evidence of implanted calcium salts or bone regeneration. Many of the marrow spaces contain very large bacilliform bodies, snugly, in short chains and clumps, particularly packing the blood vessels (Fig. 6) |
| | 60 | | | No evidence of new bone regeneration | Demineralization of carpal and adjacent ends of metacarpal. Cartilage spaces thin. No evidence of calcification or bone growth in the operative defect. *Arthritis* | Marked degeneration of carpal cartilage due to fibrous tissue overgrowth. Marked arthritis. A few small deeply staining areas are seen in the fibrous tissue, suggestive of remaining implanted calcium |
| 8. Excised carpal bone replaced with fascial bag containing salts | 30 | | | No evidence of new bone regeneration | Small area of calcification resembling bone, in the operative defect that shows definite increase in size in X-rays made 12 days apart. Cartilage spaces thin. *Arthritis* | Marked cartilage erosion by fibrous tissue, arthritis. No evidence of implanted calcium salts or new bone regeneration (Fig. 7) |
| | 60 | | | No evidence of new bone regeneration | Marked rarefaction of all carpal and metacarpal bones, loss of cartilage spaces. No evidence of calcification of bone growth. *Arthritis* | Evidence of gross infection. Discarded |
| 9. Excised astragalus, replaced by salts | 30 | | | No evidence of new bone regeneration | One small area of calcification resembling bone in the operative defect. Marked loss of cartilage from lower end of tibia. *Arthritis* | Marked evidence of arthritis, with no evidence of calcification or new bone regeneration |
| | 60 | | | No evidence of new bone regeneration | Marked rarefaction and destruction of bone of ankle joint region. No evidence of calcification in operative defect | Infected. Discarded |
| 10. Excised astragalus replaced by fascial bag containing salts | 7 | | | No evidence of new bone regeneration | No evidence of calcification or bone regeneration in the operative defect | Infected. Discarded |
| | 60 | | | No evidence of new bone regeneration | Marked rarefaction of all bony components of ankle joint. No evidence of calcification or bone regeneration. *Arthritis* | Marked arthritis of tarsal bones, with the operative defect filled with fibrous tissue and necrotic débris, no evidence of implanted calcium or new bone regeneration |

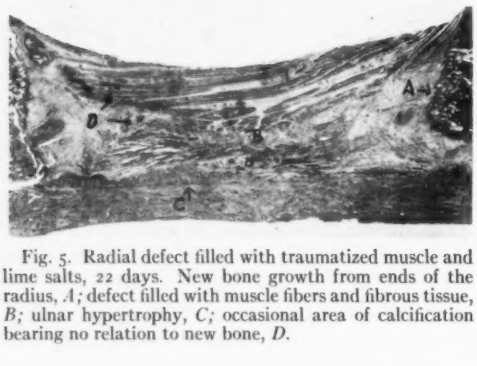


Fig. 5. Radial defect filled with traumatized muscle and lime salts, 22 days. New bone growth from ends of the radius, *A;* defect filled with muscle fibers and fibrous tissue, *B;* ulnar hypertrophy, *C;* occasional area of calcification bearing no relation to new bone, *D.*

1. A segment of one radius was excised, boiled 10 minutes, and replaced. The dogs were sacrificed in 30 and 60 days.

2. A segment of one radius was excised, fragmented, and the fragments replaced. The dogs were sacrificed in 30 and 60 days.

3. A segment of one radius was excised and the defect filled with a mixture of lime salts consisting of 85 per cent tricalcic phosphate [$Ca_3(PO_4)_2$] and 15 per cent calcium carbonate [$Ca\ CO_3$]. The dogs were sacrificed in 30 and 60 days.

4. A segment of one radius was excised, a bag made from fascia lata was filled with the same salts and placed in the defect. The dogs were sacrificed in 30 and 60 days.

5. A segment of one radius was excised, the defect was filled with a mixture of equal amounts of the salts and bits of traumatized muscle. The dogs were sacrificed in 22, 35, 45, and 60 days.

6. A carpal bone was excised, the defect filled with the same salts, and the dogs sacrificed in 30 and 60 days.

7. A carpal bone was excised, the defect filled with a fascial bag containing salts. The dogs were sacrificed in 30 and 60 days.

8. An astragalus was excised, the defect filled with salts, and the dogs sacrificed in 30 and 60 days.

9. An astragalus was excised, the defect filled with a fascial bag containing the same salts and the animals were sacrificed in 7, 60 and 90 days.

10. A segment of one radius was excised and a gelatin capsule containing the same salts was placed in the defect. The dogs were sacrificed in 30 and 60 days.

All specimens were dissected, roentgenographed, and sectioned for microscopic study.

The results of necropsy, X-ray examination and miscroscopic findings are tabulated with illustrations of typical findings (Table I).

Fig. 6. Carpal bone excised and defect filled with lime salts, 30 days. Defect filled with fibrous tissue containing no evidence of calcification or new bone growth, *A;* and carpal bones showing marked arthritis, *B.*

Fig. 7. Carpal bone excised and defect filled with fascial bag containing lime salts, 30 days. The defect is filled with fibrous tissue containing no evidence of calcification or new bone growth, *A;* and all the carpal bones show evidence of arthritis, *B.*

SUMMARY

1. The boiled bone grafts died and when inserted into defects of the radius there was no production of new bone about or within them. The only source of new bone formation in these experiments was from the ends of the radius.

2. Small fragmented live grafts similarly used were the sources of large amounts of new bone growth in each instance. Throughout the entire series of experiments wherever a small bone chip was left behind at operation, there was evidence of active bone growth from it.

3. In all cases in which lime salts were implanted in the radial defects, there was failure of regeneration of the shaft.

4. The only effect of mixing traumatized muscle and lime salts in the radial defects was to create a few areas of calcification in necrotic tissue. No regeneration of the shaft took place.

5. The only constant effect of implanting lime salts in carpal and tarsal defects was the production of a very definite proliferative arthritis. No bone was laid down in the defects.

CONCLUSIONS

1. Lime salts and boiled bone when placed into a bone defect with either traumatized muscle or fascia do not serve as a source of available calcium resulting in supersaturation of connective tissue and regeneration of missing bone.

2. Live bone chips placed in bone defects regenerate the missing bone.

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# THE USE OF SMALL DOSAGES OF PITUITARY EXTRACT IN OBSTETRICS

## A Review of the Last Twenty-two Years

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IT is now 17 years since the writer first began to use and recommend small doses of pituitary extract to induce or shorten labor (17). During this period the method has been accepted in many of the large European clinics; but in this country its employment is making only very slow headway. Yet sufficient data have now been amassed to permit a critical survey of this method, and to allow anyone with adequate obstetrical experience who is in possession of all the facts to judge for himself whether or not pituitary extract, *properly administered in small dosage*, is useful at the onset of labor or at the end of pregnancy to induce labor.

The idea of employing pituitary extract to induce labor was first put forward in Europe some 2 years before the beginning of the World War, but the use of small doses for this purpose was my original method.

In 1912 Hager administered pituitary extract during the second labor of a woman who had lost her first child because of gestation prolonged for several weeks beyond term. By inducing labor as soon as the full period of pregnancy had been reached, Hager was able to deliver a living infant, without the slightest injury to mother or child. He used a dosage of 9 minims and repeated it after 7 hours.

The next year Watson, in this country, reported the successful induction of labor in three different cases by the administration of 10 minims of extract in repeated doses; but the dosage used, though smaller than that customarily administered in the third stage of labor, was yet far larger than that which the present writer recommended in 1917.

At that time I recommended (1) the use of pituitary extract in far smaller doses than was customary; (2) the use of small dosages of pituitary extract in the first stage of labor as well as later on; and (3) the induction of labor at term by small dosages of pituitary extract.

The results in 64 cases—40 primiparæ and 24 multiparæ—were then reported. No more than 3 minims of the extract were given at any one time. After a more extended experience it was found that even smaller doses—namely 2 minims—were equally efficient, so the amount was reduced thereafter to this figure.

In 79 per cent of a series of cases in which labor was induced by such 2 minim doses of pituitary extract, which the present writer (16) reported in 1929, pains began after a single dose and delivery often took place without further injections.

### THE AUTHOR'S METHOD

The procedure I have been employing is as follows:

7 a.m., castor oil, 1 ounce.
9 a.m., pituitary extract, minims 2.*
10 a.m., pituitary extract, minims 2.*
11 a.m., pituitary extract, minims 2.*
Noon, pituitary extract, minims 2.*

*By hypodermic injection deep into thigh.

The preparation of pituitary extract I have been using during all these years is obstetrical pituitrin.[1]

When labor pains start, the injections of 2 minims are continued hourly. In successful cases, the pains generally begin after the second dose. If no pains are induced, the treatment is suspended and repeated on the third day succeeding.

Never have I observed any ill effects upon mother or child from this treatment, even when as many as ten injections were given. Apparently there is no cumulative action of the drug.

### USE OF MY METHOD ABROAD

The value of this method was quickly recognized abroad. In 1921, A. Calman (3), of Hamburg, published an account of 34 cases in

[1] Parke Davis product.

which he had administered pituitary extract according to the plan outlined in the two papers which I published in 1917 and 1920.

About the same time F. J. Browne, who had followed the teachings of Watson, presented before the Edinburgh Obstetrical Society the results of 2 years' employment of pituitary extract for the induction of labor in the venereal department of his hospital, where the use of any mechanical means of inducing labor is fraught with grave danger because in the majority of the patients a purulent discharge is present. This obstetrician was most enthusiastic regarding the method, the only drawback in his opinion being the lack of standardization of the drug—a defect which has now been satisfactorily remedied. When such standardization could be reached, he asserted: "I believe we shall be in possession of an almost ideal method for induction of labor, but even then care will be necessary, because, though the drug may be standardized, it is impossible to standardize patients. There will always remain the patient who is peculiarly susceptible to its action and probably also the patient who is entirely uninfluenced."

In 1926 Scott reviewed the literature and presented the results from a questionnaire which he had sent out to American obstetricians concerning the use of pituitary extract for the induction of labor. His conclusions were that the method was "being used much more extensively than one would gather from the literature," but "there is almost unanimous opinion among those using this method that the original dosage as proposed by Dr. Watson is too large."

The consideration accorded the method by the foreign medical literature was much greater than in that reviewed by Scott. A paper presented by J. Eversmann, in 1925, wherein he advocated the *shortening* of labor, rather than attempts to abolish its pains by the use of questionable drugs, aroused much discussion in medical circles. He reported favorably upon the present writer's method for inducing and shortening parturition and enumerated the advantages which the employment of small, repeated doses of pituitary extract has over the more massive dosage advocated by other writers. He claimed that every case in which he used this method had been successful.

Fram, in 1926, published a very favorable report on 75 cases, while a smaller series was contributed by Hoeland in 1927.

It was in 1927 that Adler also gave an account of 61 satisfactory cases; his technique varied slightly from my own.

The indications given by Adler were as follows:

1. Pregnancy prolonged beyond the natural period, because it has been repeatedly observed that the child will die if retained *in utero* beyond the normal period, even when it has been in good condition at the calculated termination of gestation. Also, if the fetus be allowed to grow larger than normal, dystocia is likely to occur when labor begins.

2. Economic considerations, which are often too pressing to be disregarded. Women may enter the hospital at term after having false pains, and be unable to remain beyond the expected sojourn because of poverty or the necessity for their presence in the home.

He considered either of these considerations sufficient to indicate the employment of a method which he had found harmless to both mother and child and which has proved efficient in such a large percentage of cases. The absolute requirement, however, is that the pregnancy must have reached term.

Hatzky, in 1928, reported a series of 117 cases of delayed labor. He felt that the figures previously offered as to the success of the method of repeated small dosage had not been based upon identical conditions. Many had used it when the uterus was completely inactive, or when the exact date at which confinement was due was not known, and their results had been meager. On the other hand, when the uterus had actually begun to contract, so that the administration of pituitary extract merely increased activity which had already been spontaneously initiated, complete success was an almost foregone conclusion. Pregnancy at term, confirmed by estimating the size attained by the fetus, *without any indications of the onset of labor*, he considers an indication in primiparæ (1) when the os is completely closed; (2) when there is

entire absence of pain, objectively perceptible, and (3) when the membranes are intact.

This obstetrician has used a number of different preparations of pituitary extract, so that his dosage has been somewhat varied on account of lack of standardization. He commonly employs injections of 0.2 cubic centimeters at one hour intervals until a total of five injections has been given, provided that labor is not increased after the first or second injection.

Hatzky concluded that my method of inducing labor has the following advantages over the use of bags: (1) no danger of complication during the course of delivery; (2) no danger of infection because of intrauterine manipulations; (3) greatly simplified technique; (4) no danger of premature delivery, the method succeeding only when the pregnancy has reached term; and (5) shortening of the duration of the parturition period. The only disadvantage cited is the uncertainty which Hatzky experienced in the effectiveness of the injections in producing labor pains. This may have been due in part to differences in the pituitary extract employed, since it is well known that there are wide variations in the potency of various commercial preparations.

Widera, another German writer, who used the method in 44 cases in his obstetrical service at Oppeln, is very enthusiastic about this method. He had 75 per cent of complete successes, using 3 units per cubic centimeter of the Voegtlin preparation of pituitary extract at a dose, the injections being given every 15 minutes until strong, regular pains began. In his 44 cases, 33 labors began with satisfactory promptness, only two requiring repetition of the dosage when the first series failed to bring results. There were 11 failures.

A still later report is that of La Haye and Peters, who had tried the method in 19 cases at the Strasbourg Obstetrical Clinic. From their experience in this small series, they decided that the method is most excellent, if certain conditions are fulfilled.

One of the patients of La Haye and Peters showed an intoxication by the drug, this being the only case of idiosyncrasy to pituitary extract which I have heard of during 17 years' experience with the method. When she had been given 9 small injections, this woman developed clonic spasms of the diaphragm, resembling hiccough, which seemed to have no relation to the uterine contractions. The injections were stopped, but when labor pains ceased were renewed once more after an interval of an hour and a half. After the seventh injection of the second series, the spasms recurred, but the labor pains were rhythmic and strong and delivery was promptly accomplished. The diagnosis of drug idiosyncrasy was confirmed by eye signs, which included the development of a transient amaurosis, a pronounced myosis with disturbance of accommodation, and feeble response to light. Tendon and cutaneous reflexes remained normal. Delivery was accomplished shortly before midnight, but the hiccough continued for the remainder of the night. The following day, however, it had quite disappeared and no return of the trouble occurred.

The latest reports are those of Dueckelmann made in 1931, and of Hellendall which came out in March, 1932. Their favorable results demonstrate that the popularity of the method continues to increase in European obstetrical practice.

### THE PROPER DOSAGE

Despite its wide acceptance in Europe, the method of inducing labor at term by small repeated doses of pituitary extract has not received the recognition in this country that it deserves. This is due to a prevalent fear that pituitary extract given prior to the expulsion period may cause violent uterine contractions and possible rupture of the uterus.

In my own experience and that of practically all European observers, no such danger exists when a dosage as small as 2 minims is employed. True, Mendenhall, in 1929, accumulated from the literature 89 cases of ruptured uterus from the use of pituitary solution reported from 1913 to 1927. Yet an analysis of his series shows that, in the great majority of cases, the dosage either was not stated or was entirely too high.

Refuting Mendenhall's article in 1930, I pointed out (15) that the crux of the situation is the dosage of pituitary extract employed.

Nobody can deny the danger of injecting 1 cubic centimeter before dilatation of the cervix, but abundant clinical experience proves the safety of such small doses as 0.2 cubic centimeter.

## SUMMARY

The preceding review of some of the reports from European obstetric services leaves no doubt of the general satisfaction which the method of inducing labor by repeated small doses of pituitary extract, as described by the author in 1917, has given to a large number of clinics as well as practitioners. It is to be regretted that the method has not found a wider application in the United States. Not one of the writers who have been reviewed has noted any evil effects upon either mother or child. In not one of the complicated cases, or even those in which fetal death occurred, could the outcome in any way be attributed to the use of the drug. The percentage of complications is, if anything, lower in the cases in which pituitary extract was used to induce labor than in those in which other methods of induction were employed, or even in those in which the pains occurred spontaneously.

It is to be hoped that American obstetricians will be inclined to employ the method more often as, combined with the judicious administration of nitrous oxide anæsthesia in the second stage, it provides a safe and efficient means of delivery, which will go far to satisfy the continued demands of the modern woman that she be relieved of the age-old burden of the anguish of maternity.

The method is again fully described. After 17 years' use, the author's technique has not been changed; and, in the opinion of those who have used it, it still remains the best procedure for inducing labor at term.

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# ADAMANTINE TUMORS OF THE JAWS[1]

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ADAMANTINE tumors have been reputed to be surgical curiosities and have not occasioned as much study as their incidence and malignant potentialities warrant. Most recent writers concur in the opinion that such growths are probably more frequent than the literature on the subject indicates. Undoubtedly many patients with such tumors have been treated without being reported, and others have been operated upon with an inadequate diagnosis. This applies especially to the small unilocular lesions, which may be mistaken for radicular or dentigerous cysts. The primary purpose of this paper is to present a plan of treatment which seems rational to us, as well as to give a brief review of the clinical course and pathological aspects of the lesion.

Vorzimer and Perla credited Guzack with the first description of a cystic tumor of the lower jaw in 1826. Kegel (23) thinks that the history of the adamantine tumors dates from 1868, when Broca published his memorable report on a new group of tumors which he designated as "odontoma." Since that time many different terms have been applied to this neoplasm. Murphy believed that Borst was the first to suggest the term adamantinoma, whereas Vorzimer and Perla date the first full description of the tumor from Falkson's paper published in 1879. Since that time numerous designations have been applied, including adamantine epithelioma, cystosarcoma, adenocarcinoma, epithelial odontoma, cystoma, cystic tumor of the jaw, multilocular cyst of the jaw, adamantine tumor, chorioblastoma and ameloblastoma.

Classifications of tumors of dental origin have been grossly inadequate. This is due in large part to the variance in opinion as to the histogenesis of these neoplasms. Wohl suggests that they be classified either as products of inflammation, or as derivatives of the tooth germ.

Several excellent résumés on the subject of adamantine tumors are offered in the literature. In 1910 Lewis collected 70 cases, including 3 of his own. In 1916, Wohl brought the total up to 82 by adding 4 original cases and including the 8 reported by New. In 1924 Murphy estimated that 100 such tumors had been collected. In 1932 Kegel cited 35 cases in which patients had been referred to the Johns Hopkins Hospital for diagnosis or treatment.

Adamantine tumors, as in other types of neoplasm, may be classified in different ways, but the usual criterion is on the basis of the growth being either unilocular or multilocular. The tumor is characteristically composed of many cystic areas, although there is a fairly large group of cases in which only one cyst is present. The diagnosis of unilocular cyst must be made with caution, because in some of these growths the gross picture is one of a single large cyst, whereas in reality many smaller cysts exist. Obviously this point is of considerable significance in determining the type of operation to be performed.

Another classification of these tumors is on the basis of whether they are solid or cystic. No sharp differentiation can be made on this criterion, since many intermediate cases are found, in which one part of the tumor is solid and another part cystic. Whether a given tumor is solid or cystic, or whether it is composed of a single cyst or is multilocular, carries considerable prognostic import, as will be discussed later.

The size of the adamantine tumors is quite variable. It should be borne in mind that these are central expansive growths, and for this reason they are not observed early in their course, and have usually attained considerable size before advice is sought. The silent central nature of this neoplasm does not make for early diagnosis. Many large tumors have been reported. Ewing speaks of an adamantinoma coming under his observation which was as large as the head of a child, and weighed 1.5 kilograms. If these tumors made their presence known earlier their nature would undoubtedly be better understood.

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The age at which patients come under the observation of the physician or dentist is subject to wide variation. Massin has reported the earliest case on record, an adamantinoma occurring in a newborn infant, together with a detailed microscopic description of the tumor. The oldest case in Lewis' series occurred at the age of 75 years. The decade showing the highest incidence in Simmon's series was between 20 and 30. Kegel (23) gave the age at which the tumor was first noted as between 11 and 35 years. In another paper the same author (22) stated that the time the adamantinomata usually appear is between the ages of 15 and 25, roughly the time of the second dentition. New had previously propounded the same doctrine. He noted that the average age for adamantine tumors to appear in the lower molar area was 33 years, whereas the average age for such neoplasms in the cuspid region was between 16 and 17 years of age. He was of the opinion that tooth eruption may play a part in the production of adamantinomata through the rôle of irritation. Both the cases to be reported by us occurred between the ages of 15 and 20 years. Ewing expressed the opinion that the process begins much earlier than is generally recognized, but due to its prolonged nature the growth may not be noted until middle, or even late, life. Lewis gave the time elapsing from the time of the initial symptom or sign of the condition until removal of the mass as 8½ years. Simmons concurred with an average duration of 9 years. Extremes have been reported. Eve reported a rapidly growing tumor of only 13 weeks' duration, the patient dying of a complication rather than directly from the tumor. Frantz and Stix reported the other extreme, a patient who had been subjected to jaw resection in 1878 and who died in 1929, the tumor having recurred and been present for 51 years. Murphy stated that the semi-solid tumors evolve in from 1 to 15 years; the purely cystic in from 10 to 20 years; the unilocular type averages 10 years in its development before surgical advice is sought; and the multilocular develops in 14 to 15 years. Kegel (23) thought that in some cases the progress of the tumor seems to be accelerated by tooth extraction. Murphy stated that the solid type of adamantine tumor predominates in early age, and that it rarely occurs after the age of 30. Conversely the cystic type is more frequent in later life.

Kegel (23) and Graves considered the adamantinoma to be more common among the black than the white race. Westmoreland, in a series of poorly described cystic tumors of the jaws, noted a very marked predilection for such tumors to occur among negroes. Blair and Brown thought this neoplasm to be more common in females than males.

As to the most frequent site of this tumor, opinion is unanimous. The lower molar region is by far its most frequent location. Aschoff stated that the molar and premolar areas are the most common sites of occurrence. Broders and MacCarty stated that these neoplasms are usually found near the angle of the mandible. In the series of 21 cases reported by Steensland the location was given in 20 cases. Of these, 17 were in the lower jaw, 2 in the upper, and in 1 case adamantine tumors occurred simultaneously in both the maxilla and mandible. In 1915, New collected 9 adamantinomata of the upper jaw, 2 of which were his own. Kegel (23) found 19, in his series of 35 to be located in the lower jaw, only 2 being located anteriorly. Suker was not in accord with most writers, in that he considered the most frequent site to be the upper jaw or antrum. Ewing and Murphy agreed that the solid adamantine tumors are more frequent in the upper than in the lower jaw, and Ewing was of the opinion that the upper yields more of the malignant adamantinomata than does the lower jaw.

Adamantine tumors are also found in other locations than the jaws. Such growths comprise a fair percentage of the sellar and parasellar growths. Peet credits Onanoff with first noting the resemblance between these hypophyseal tumors and those of the jaws, in 1892. Frazier and Alpers present 14 adamantinomata in a total of 244 tumors of that region. Peet reported 3 adamantinomata of the pituitary region, and stated that the majority of such afflicted patients present the Frœhlich syndrome. Carson and Hellwig reported such a suprasellar tumor and an astrocytoma in the same patient. Adamantinomata occurring in

the pituitary region are thought to be derived from cell rests of the embryonic hypophyseal duct. In 1931, Suker reported a case of squamous cell carcinoma of the orbit which he considered to be a metamorphosis of an adamantinoma. There is no other instance in the literature in which such a tumor originated in the orbit, although some have involved the orbit by extension from the antrum. Another poorly understood adamantinoma is that which is reputed to occur in the tibia. Three such cases have been reported. Ryrie thought the structure of these tumors possibly justified the diagnosis of adamantinoma. It would appear highly improbable that these tumors arise from a tooth germ. Ryrie said that those of the tibia are "best considered of basal-cell carcinoma of traumatic origin, having their basis not in congenital cell rests, but in the passage of a constantly frustrated reparative hyperplasia into neoplasia in a special environment of the tissue reaction." Fischer was of the opinion that the developing enamel organ of the embryo is not transferred from the oral cavity to the tibia, but rather that the growth can best be accounted for by an excessive development of the multipotent embryonic ectoderm of the leg, and its differentiation in the direction of enamel formation. Baker and Hawksley did not consider this growth to be teratomatous in origin, because of the absence of other tissues, but thought that the epithelium retained its basal cell potentialities and is stimulated to growth by injury. If we accept these tibial tumors as true adamantinomata we must either alter our concept of their histogenesis, or search for a more tenable hypothesis as to the development of adamantine tumors of the jaws.

It is generally conceded that the adamantinomata are of epithelial origin, although Broca favored the theory that they arise from the mesoderm. According to the most widely accepted theory these growths are of epithelial origin.

Three possible methods of development are propounded at the present time: that adamantinomata arise from *débris épithéliaux paradentaires;* that such tumors are developed directly from the tooth germ; and that they are derived directly from the alveolar epithelium. The first hypothesis was first propounded in a classic paper by Malassez, in 1885, and is the most widely accepted theory at the present time. It was endorsed by Ewing, Bump, Suker, and others. Malassez found masses of epithelial cells along the peridental membrane from the gingival margin to the apex of the root. He considered such cell groups to be derivatives of the enamel organ, and designated them as paradental epithelial débris. Sometimes such cell masses were observed outside the alveolodental ligament, in the jaw bone. This author considered such cell aggregations to be analogous to the rich dental apparatus of some of the lower vertebrates, and thought them to be related to the supernumerary teeth of the third dentition. Simmons stated that such tumors arise from remnants of the enamel organ, or from the paradental epithelial débris. Murphy brought out the fact that statistics show the development of these tumors is not directly related to the development of the teeth, thus opposing Broca's follicular theory, and upholding Malassez' rest theory. Kaufmann also ascribed the development of the adamantinoma from rests of the enamel organ. Jordan has shown that remnants of the outer cell layer of the enamel organ frequently persist, and are to be found in relation to the inner margin of the bony alveolus, the wall of which is produced by intramembranous ossification in the connective tissue surrounding the embryonic dental sac.

The second theory of origin of the adamantinomata considers these tumors to arise from additional tooth germs. This thesis holds that the adamantinoma arises from the neoplastic transformation of the tooth germ. Falkson has been one of the keenest exponents of this hypothesis. If we assume that these neoplasms owe their origin to neoplastic transformation of the tooth germ, we might reasonably expect such tumors to be associated with faulty tooth formation in a fairly high percentage of cases. Two of the cases of New's series were associated with unerupted third molars. In one of our cases there was a supernumerary tooth in the maxilla. Curiously, supernumerary symmetrically placed teeth, and absence of teeth, are not common

findings. If the tumor owes its origin to the neoplastic transformation of the tooth germ of a supernumerary, or even one of a permanent tooth, we might reasonably expect to find a similar symmetrically placed tooth on the opposite side of the mouth, in at least an occasional case, or failure of development of the full quota of teeth in the second instance.

The third theory of origin holds that the adamantinoma arises from the mucous membrane of the oral cavity, or from the mucous glands of the mouth. Broders and MacCarty found one such tumor which showed a direct connection with the epithelium of the gum through the medium of epithelial columns. This observation suggested to them that the neoplasm arises from the regenerative or basal cells of the epithelium of the mucous membrane, which would be in accord with all other types of epithelioma. Ewing has also noted such a connection, but favors the theory of Malassez as to the origin of the adamantinoma. Bland-Sutton subscribed to this theory of origin. Kegel (23) thought, however, that the adamantine epithelium invades the oral epithelium in the exceptional case which shows continuity between the tumor and the mouth, rather than being derived from it. Horsley drew attention to the fact that the clinical course of the adamantinoma is quite different from that of basal cell cancer.

Lewis quoted Bland-Sutton as stating that many of the multilocular cystic tumors of the jaws are in reality endotheliomata.

Like most slowly growing tumors, the early symptoms are nil, which accounts for the prolonged period elapsing before the patients come to surgery. Pain is not a common symptom, and the one thing which brings these patients in for advice is deformity of the jaw, or even of the face. Occasionally a cystic tumor ruptures into the oral cavity and discharges its content, the opening often healing spontaneously, only to rupture again at a later date. Occasionally the tumor becomes infected and in that case the picture is one of an osteomyelitis. The presence of a loose tooth is sometimes the initial complaint. The history of early extraction is common. The tumor distends the tissues until only a thin bony shell is present, giving a parchment-like bony capsule which crepitates on pressure. The contour may be regular or lobulated. Pathological fracture sometimes occurs. In advanced cases the tumor may impinge on adjacent structures, giving rise to pressure symptoms. Phonation and mastication are sometimes embarrassed in the case of large tumors, and in such lesions of the maxilla the eye may be displaced by the growth. The absence of infiltration about the tumor, and the lack of fixation are important diagnostic criteria. The regional lymph glands are usually not palpable, except in those cases in which the tumor is infected. Bony or fibrous trabeculation is commonly present. The cysts usually contain a thin yellow or brown fluid, although it is occasionally viscid, and cholesterin crystals may be present. Ewing thought the calcific particles sometimes found are probably remnants of imperfect enamel.

On roentgen examination the adamantinoma appears as a central bone expansive tumor, the outline is clearly defined, and there is no periosteal reaction. The tumor may be monocystic or multilocular, and the so called honeycomb appearance is commonly seen.

### MICROSCOPIC APPEARANCE

The epithelial constituents of the tumor are by far the most enticing for study. Several types of epithelial cell may be present. Kruse described three microscopic types of adamantinoma, based on different stages in the development of the enamel organ. Lewis considers the cylindric type to be the most characteristic cell of the adamantinoma, although the polygonal and the stellate epithelium aid in classification of such tumors. All gradations of epithelial cell from the stratified squamous to the specialized adult enameloblast are seen, and often all stages between these extremes are seen in the same tumor. The epithelium may be all of one type, but more commonly more than one type is present, one or the other type predominating. Broders and MacCarty describe two distinct types of cell: the outer, or columnar cells, which they consider to be of the regenerative type, and correspond to the columnar germinal or regenerative cells of the enamel organ; and the polygonal and stellate cells which are so characteristic, and

represent an advanced stage of differentiation. They also sometimes contain prickles. The peripheral columnar cells are arranged radially in a palisade layer, while the stellate cells are placed more centrally. Ewing described three main types of adamantinoma. All three types are locally aggressive, and he places them in the general class of carcinoma. The adenocarcinomata, or glandular tumors, exhibit chiefly one structure, whereas the other types show extreme and sharp variations in cell type, and the arrangement of the cells is quite diverse. In the first type, the acanthoma, anastomosing cords of squamous epithelium are present, in which are spine cells and pearls. In isolated areas cells showing the characteristics of the enamel organ appear. The second type is the plexiform epithelioma, showing broad convoluted columns of epithelium with no marked tendency to squamous formation. The third type is the glandular form, and here the columnar enameloblasts predominate. Often the columnar cells enclose areas of reticulated cells. Numerous pearls may be surrounded by reticulated cells, and these in turn be surrounded by the columnar cells. In recurrent tumors the cells tend to lose their original identity, and may eventually appear as a large round cell, perivascular growth with no trace of the original epithelial origin. Aschoff described the formation of typical enamel, Wohl has observed dentine formation, and Kegel spoke of both dentine and cement being found in such tumors. Fully formed teeth are sometimes observed in such cysts.

The stroma of the adamantinoma shows a wide range of variation, and the proportion of epithelium to connective tissue also fluctuates widely. It may be cellular, or very dense and of a hyaline nature, as in the gubernaculum dentis. In the stroma of some of these tumors may sometimes be found a structure identical with that of the giant cell epulis and giant cell tumor. Portions of cement or bone may appear. Sometimes the stroma becomes exceedingly vascular. Mucoid changes occur, as well as cirrhosis and calcification. Bump speaks of cases in which the stroma growth exceeds the epithelial, giving the appearance of a sarcoma, and Papadimitriou presented a case for which he used the term adamantinoma sarcomatodes, a tumor characterized by very rapid growth. He did not consider this stroma to be malignant clinically.

Thus far no definite criterion has been established for judging the malignant potentialities of a given tumor from a study of its microscopic appearance. Simmons has suggested that the degree of malignancy probably varies with the degree of differentiation of the cells. Kegel thought that no grading according to degrees of malignancy can be made on the basis of the microscopic picture, as to rapidity of growth, duration, or recurrences. Ewing considered the solid tumors to be more cellular and more malignant than the cystic variety. In the case of 51 years' duration reported by Frantz and Stix the sections showed an alveolar arrangement, the peripheral cells being of the columnar type and arranged radially in a palisade layer, with central cells of the stellate type.

### DIFFERENTIAL DIAGNOSIS

The adamantinoma is a central expansive growth, and must be differentiated from similar tumors occurring in the jaw bones. The differential diagnosis of intracranial adamantinomata will not be considered in this paper.

Dentigerous cysts occasionally offer considerable confusion in the differential diagnosis from adamantinomata, especially in view of the fact that dentigerous cysts often occur in the lower molar region, and because a monolocular adamantinoma may be associated with an unerupted tooth. Another confusing factor is that cases have been described of dentigerous cysts with a lining of adamantine epithelium. Bloodgood in 1905 reported such a finding on Barrie's case. More recently, however, there is a trend to more properly consider these tumors as adamantinomata. The dentigerous cyst is lined with stratified squamous epithelium.

Radicular cysts ordinarily offer no great diagnostic problem, but there are cases in which the cyst attains large size and apparently loses its connection with the non-vital tooth from which it originated. The finding of vital teeth in the region of such a tumor obviates the diagnosis of root cyst. This

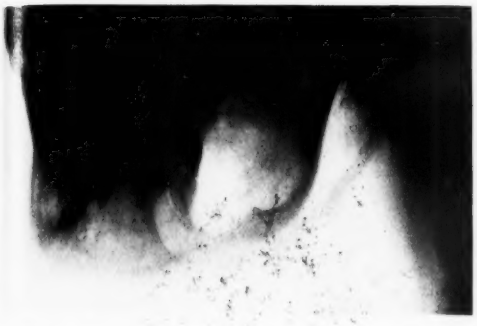

Fig. 1. Roentgenogram showing large unilocular cyst.

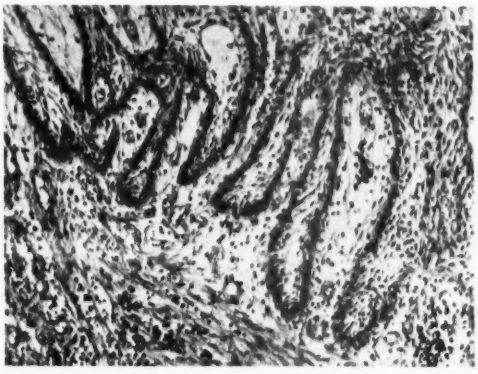

Fig. 2. Photomicrograph showing columnar cells arranged radially in palisade manner.

tumor is often found in the upper lateral incisor area.

The giant cell tumor is one of the most difficult conditions to differentiate. It occurs very frequently in the lower molar area. Because of its trabeculation it may simulate an adamantinoma of the multilocular type. Giant cell tumors are much more rapid in development, however, and if X-ray therapy be used as a diagnostic procedure, it will be found that the giant cell neoplasms are much more responsive than the adamantinomata. If the duration of the tumor is unknown, and if either condition is at all atypical, a biopsy is often necessary to establish the true nature of the growth.

Adamantinomata of the upper jaw are often diagnosed as carcinoma of the maxillary sinus. Even on microscopic examination an undifferentiated tumor may suggest carcinoma, when in reality we are dealing with an adamantinoma. The important points in the differential diagnosis are: lack of the parchment-like crepitation in case of carcinoma; shorter duration of the carcinoma; age incidence of carcinoma is later than that of adamantinoma, as a general rule, although there are exceptions in both directions; and, mitotic figures are not seen in adamantine growths.

As already intimated, adamantine tumors in which the growth of the stroma is greatly out of proportion to that of the epithelial constituents, may simulate sarcoma. Here again, in sarcoma, as in carcinoma, parchment-like crepitation is absent, the sarcomatous process is much more rapid in its evolution, and mitotic figures are present.

Adamantinoma may also sometimes be confused with an osteoma or fibroma. Kegel (23) noted that some adamantine tumors may resemble polycystic osteitis fibrosa. Wohl considered endothelioma and myeloid tumor in the differential diagnosis.

Opinion is variable as to the proper treatment of these tumors. All writers agree on one point, and that is that surgery is the proper therapy. X-ray and radium have not received much attention in the literature as a form of treatment. Lewis noted that in one of his cases massive doses of X-ray decreased the size of the tumor somewhat. In 1927 Bump stated that up to that time the X-ray had not cured an adamantine epithelioma. In 6 cases Kegel (23) used the X-ray or radium and noted no beneficial results from them. Simmons mentioned 1 case which showed temporary improvement following radiation. In one of his cases he used radium in repeated recurrence of the tumor, and the patient died from local extension of the neoplasm to the brain.

The majority of writers favor radical treatment of these tumors, advocating resection of the jaw. In 10 of the 12 cases reported by Simmons some previous form of conservative treatment had been carried out. He advocated jaw resection as the method of choice in the treatment of these tumors, especially if

Fig. 3. Original roentgenogram of multilocular adamantinoma, trabeculæ are well defined.

Fig. 4. Roentgenogram 1 year after operation.

the cuboidal type of epithelium is predominant, or if the tumor is very large. He also felt that metastasis is more common than is generally supposed. In the series of 35 cases reported by Kegel, 19 recurred, and if the cases were excluded in which radical primary resection was performed, the incidence of recurrence was 79 per cent. Nevertheless, this author favored curettage followed by the thermal or chemical cautery when the tumor is monocystic, and in cases in which the lesion is a solid one with an intact bony shell. He also favored subperiosteal resection in selected cases. The polycystic adamantine tumors, however, he thought are best treated by jaw resection. He noted that the recurrent tumors are more difficult to eradicate than the primary ones. Ewing noted, also, that the multilocular cysts often require sacrifice of the jaw bone for their eradication. Lewis favored wide resection, since he considered these tumors practically impossible to enucleate. New likewise subscribed to resection of the jaw bone.

Ewing considered the superficial tumors and the small cysts to lend themselves readily to extirpation. Bloodgood advised conservative treatment, realizing that recurrence is common.

It is generally conceded that the prognosi of the solid tumors is not as good as that o the cystic variety. Murphy favored mor radical surgery in the solid and semi-soli types than in the cystic adamantinomata.

The recurrent tumors often exhibit distinc cell differences from those of the parent tumor, as Ewing pointed out, the recurrences often show marked anaplasia. Malignancy often occurs in such a tumor after recurrence. It is generally conceded that metastatic involvement from adamantinomata of the jaw are unusual, although Simmons considered them to be more common than generally supposed. In one of his cases there was lung metastasis and in two cases there was glandular involvement. In a fibroepithelial tumor mentioned by Ewing, metastases were observed in a cervical node and a small nodule in the lung; in another of his cases the fourth recurrence was in the cervical nodes and loose cervical tissues, and probably in the lung. Vorzimer and Perla reported a case in which five operations were performed eventually with the jaw resection, with eventual metastasis to the lung. This case is peculiar in that the lung tumor was considered to be benign and not malignant, and was accounted for on the basis of aspiration of adamantine tissue at the time of one of the

Fig. 5. Photograph of resected section of mandible.

operations. The tumor grew primarily within the lumina of the bronchial tree. Eve reported a case in 1883 in which a patient died of pneumonia following operation for an adamantinoma of the lower jaw, the mass being only of 13 weeks' duration. Here the lumbar glands showed the "exact prototype of the primary growth." Kegel (22) maintained that when the adamantine tumors are left alone they never metastasize, and Bloodgood thought that they do not metastasize in the true sense of the word, but that implantation metastasis in the soft parts may follow their incomplete removal.

CASE 1. This tumor occurred in a white boy, aged 17 years. The history was negative until a few days before he sought advice, when he noticed a "swelling" in the region of the left ramus of the mandible. He consulted his dentist who made an incision over the occlusal aspect of the mass, evacuating a large amount of thin yellow fluid. The patient was referred for surgery. The X-ray (Fig. 1) showed a large unilocular cyst extending forward as far as the first molar area, and posteriorly almost to the posterior aspect of the ramus. The tumor extended into the coronoid process, but the condyle was not involved. Operation was performed December 27, 1932, the tumor being thoroughly curetted and the anterior part of the internal pterygoid muscle resected, since the tumor extended backward between that muscle and the ramus of the mandible. Two weeks subsequent to operation radium treatment was instituted. To date there has been no recurrence of the tumor and the cavity has been largely replaced by new bone. The patient is symptom-free except for an area of anæsthesia over the distribution of the mental nerve, caused, of course, by the removal of that segment of the mandibular nerve traversing the tumor.

Microscopically the epithelium is arranged in an orderly fashion. Columnar cells arranged radially in

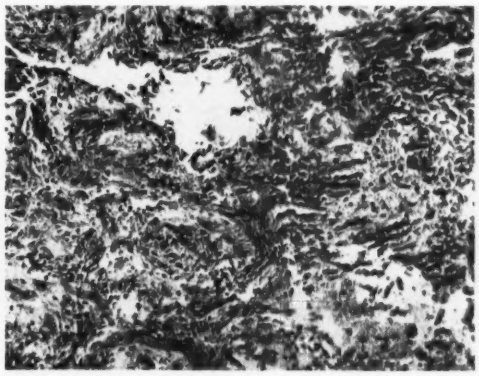

Fig. 6. Photomicrograph showing the predominance of cuboidal type of cells.

a palisade manner, with the characteristic stellate cell are seen (Fig. 2).

CASE 2. The second tumor occurred in a white girl 15 years of age. She had been treated elsewhere by conservative treatment (curettage) one year prior to consulting one of the authors. She complained of no symptoms at any time during the illness except the presence of a lump in the lower right molar area. Figure 3 shows the original X-ray picture of the tumor, revealing a multilocular adamantinoma, with well defined trabeculæ.

Errors of dentition are not especially common in cases of adamantinoma. There was no anomaly of the lower molars in either of these cases, except that in this case the crown was in a transverse position, and placed posteriorly, probably due to the pressure occasioned by the tumor. In this case, however, the X-ray revealed the presence of a transversely impacted supernumerary tooth opposite the apex of the upper right second bicuspid. At the primary operation (done elsewhere) the trabeculæ were well broken down and the cavities thoroughly curetted, but no electrocoagulation and chemical or thermal cauterization were employed. The tumor rapidly recurred and when seen 1 year later, it entirely filled the artificially formed monocystic cavity. The X-ray appearance at that time is shown in Figure 4.

Conservative operation was done a second time, on December 3, 1932, the tumor thoroughly removed by curettage, and electrocoagulation employed over the remaining tumor-bearing cavity. About 2 weeks after operation radium and deep X-ray therapy were instituted. There was considerable reaction to the radium. Five weeks subsequent to operation the patient developed scarlet fever, but recovery was uneventful, without complication. Because of persistent adenopathy, and the fact that the recurrence previously had been rapid for this type of tumor, it was deemed advisable to resect the mandible together with the cervical glands. This was done March 15, 1933. Recovery was uneventful and to date there has been no evidence of recurrence. The

resected section of mandible is shown in Figure 5. Bone grafting will be done later.

The microscopic sections of this tumor show bizarre patterns. Few cylindric cells are present and the cuboidal type predominates. A few whorls are present (Fig. 6).

The factors of primary interest to the authors are the possible histogenesis of these adamantine tumors, and the type of treatment best suited for a given case.

In both our cases the full quota of permanent tooth germs are represented by well developed teeth. The only point in favor of the theory that the adamantinomata develop directly from the tooth germ is the fact that in Case 2 there was a well developed supernumerary impacted tooth in the upper jaw. We feel that the theory advanced in the classic work of Malassez is most tenable at the present time, although the other theories are not disproved.

The question of treatment is of utmost importance. In dealing with this phase of the problem we must remember that, from a clinical standpoint, there are several distinct types of the tumor; that the microscopic features show wide variance in different tumors; that the tumor is a slowly growing one; that the first recurrence is not malignant as frequently as most writers would have us believe; and finally, that if malignancy does supervene, the incidence of metastasis, or even of cervical node involvement, is fairly low.

The small unilocular cystic tumor offers the best chance for conservative therapy. By conservative treatment we mean the thorough curettage of the tumor mass, with adequate coagulation of the entire cavity by electrosurgery. This necessarily implies free access to the entire tumor-bearing area. We feel that radium should be used after operation as a prophylactic measure, realizing that these tumors are not very reactive to this form of therapy. Another type of tumor which we feel can be best treated by conservative surgery is the multilocular tumor in which the loculi are few in number, and of such size as to be readily exposed to the treatment described, all trabeculæ being broken down. Lesions similar to that in Case 2 can be adequately treated by this method, provided the cell differentiation is sufficiently far advanced, as discussed below. On the contrary, we feel definitely that radical surgery, in the form of jaw resection together with resection of the regional lymph glands, is to be advocated in those tumors which present numerous ill defined cysts, a condition in which all parts of the tumor are not easily exposed and free of access. The honeycomb tumors, with numerous small scattered loculi will come in this category, regardless of the degree of differentiation of the cells.

We believe that all tumors, whether multilocular or unilocular, should be treated by jaw resection if the epithelial component shows little or no differentiation of its cells. This statement may bear correction in the future and should be made with a certain degree of reservation, since the correlation of the microscopic appearance of the tumor with the degree of potential malignancy is not to be gleaned from the literature in a sufficiently large series of cases to draw too definite conclusions.

We feel that the duration and size of the tumor are very definite factors to be taken into consideration in determining whether or not the therapy be conservative or radical. Obviously, the rapidly growing tumors, such as those which develop within a few weeks, should be treated by jaw resection at the outset. The very large tumors, in which there is marked deformity of the jaw, also require resection.

Adamantine tumors of the maxilla require more radical surgery than those of the mandible. There are two reasons for this. First, maxillary tumors are more often of the solid type than those of mandibular origin. Second, although these neoplasms probably are no more prone to metastasis than those of the lower jaw, it is possible for the growth to extend by continuity into the orbit or base of the skull.

Were the recurrences malignant in a large percentage of cases, or were the percentage of metastases high, the authors would concur with those advocating radical surgery in the treatment of adamantine tumors. Since such is obviously not the case, as judged by the literature on the subject, we recommend the suggestions cited.

## CONCLUSIONS

1. Adamantine tumors of the jaws are undoubtedly of much greater frequency than the literature would have us believe.

2. The histogenesis is best explained by the theory of paradental epithelial rests, which occasionally take on the potentialities of their ancestors, giving rise to the adamantinomata.

3. The explanations for the great frequency of such tumors in the lower molar region seem inadequate.

4. Conservative treatment should be adopted in unilocular adamantine cysts, especially if the epithelium is well differentiated, and the tumor has been slow in development. The conservative treatment consists in curettage following free exposure of the cavity or cavities, electrocoagulation of the tumor-bearing area, with possibly subsequent radium therapy.

5. Radical excision of a segment of the jaw should be done in polycystic tumors, when the cysts are small, ill defined, and not easily exposed to ready access. Radical measures should also be adopted in most adamantine tumors of the upper jaw, in many tumors of the solid type, and in cases showing undifferentiated epithelium. In the latter we favor radical treatment at the outset, at least, until sufficient cases have been reported correlating the microscopic picture with the clinical course of the lesion.

6. Radium and deep X-ray therapy are of very questionable value, but we still use radium after operation as a prophylactic measure. It is possible that we shall discard it later, but not for the present.

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# THE EFFECT OF MECHANICAL STIMULATION OF THE NIPPLES ON THE OVARY AND THE SEXUAL CYCLE

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IT is well known that the sexual cyclicity is interrupted during lactation, but no satisfactory explanation of this fact has yet been offered. In a recent publication, Freund discusses the problem of lactation amenorrhœa, and from observations of his rich clinical material he concludes that the reappearance of menstruation during lactation is a result of the decrease in the activity of the mammary gland. Since we have shown in our previous communications (3, 4) that the mere stimulus of suckling inhibits sexual cyclicity in the rat (even after the main milk ducts of all nipples have been cut, and escape of milk has thus been made impossible), we would be inclined to think that lactation amenorrhœa in humans is also conditioned by the nervous stimulation of the nipple rather than by the secretory activity of the gland. In a more recent experimental series, we tried to establish whether the mechanical stimulation of the nipples by nursing would also inhibit the sexual cyclicity of the normally estric, non-lactating adult rat.

Briefly, under the influence of the suckling stimulus, we observed a diestrus of about 16 days' duration during which the uterus became progestational in appearance with frequent formation of placentomata, and numerous alveoli appeared around the mammary ducts (5).

In the present paper we describe the effects of exposing normal animals to such a stimulus for a long period of time, and the repetition and extension of our original observations upon the mouse.

Before proceeding with the discussion of our work, we should like to draw attention to the large number of animals required in the investigation of this problem. While the suckling of an active litter is the only satisfactory method of stimulating the nipple, a large quantity of experimental material must be available if litters of the right age are to be obtained. Furthermore, such litters are undernourished, and therefore of little use for other work. This is why, in spite of the large size of our own rat and mouse colonies, we are able to report results only on a limited number of animals. We feel, however, that these results are of such a nature that one may safely base discussion on them.

Two adult female rats, seen to be normally cyclic for some time following the weaning of their own litters, were exposed to a strong suckling stimulus and the young kept alive by exchanging them on alternate days with the well nourished litter of a normally lactating mother, the young of the normal mother being transferred on these days to the experimental animal. In one of these animals this was done for a period of 10 weeks and in the other for a period of 7 weeks. The sex changes were followed by daily examination of the vaginal smears and biopsy sections were taken of the mammary glands from time to time.

With the onset of suckling the first of these animals went into a diestrus which lasted for 17 days. On the 18th day the smear, showing only cornified cells, indicated estrus; but on the following day the animal went into a second period of diestrus which lasted 27 days. Again there was a day of estrus, followed by a third diestrus of 23 days. Estrus appeared once more; then a fourth diestrus, on the sixth day of which the animal was killed.

The second animal behaved similarly, showing three successive periods of diestrus, separated the one from the other by a day—or in one case 2 days—of estrus. They were of 16, 16, and 15 days in length, and the animal was killed at the third appearance of estrus.

The mammary glands showed, in the earlier stages, changes such as we described in our previous paper. The glands at the middle of the first diestrus were found to be those typical of early pregnancy—numerous alveoli

with no secretion. But 4 days before the appearance of the first estrus, secretion had begun and at estrus sections showed a fully developed and lactating gland. These results are perhaps more obvious from Figures 1, 2, and 3.

That such lactation was not subnormal was indicated by the ability of these rats to maintain normal sized litters at those periods when the glands were fully developed.

During the diestrus period, the ovaries showed a single set of large corpora lutea similar to those seen during the earlier stages of normal lactation. The peri-ovarian capsule was greatly distended with fluid (Figure 4). The hypophyses of these animals were considerably enlarged. The adrenal cortex showed a marked increase in size and a large number of cysts, which were filled with eosinophilic colloid (Fig. 5).

In an attempt to repeat this work on mice, we gave litters to 11 animals Technically this offered little difficulty, for suckling occurred in almost 100 per cent of cases, and no animals had to be discarded because of necrosis of the nipples. The methods of nourishing the young and of following the sex cycle and mammary gland changes were identical with those used on the rat.

We observed in all cases the cessation of estrus and development of the mammary gland as previously described.

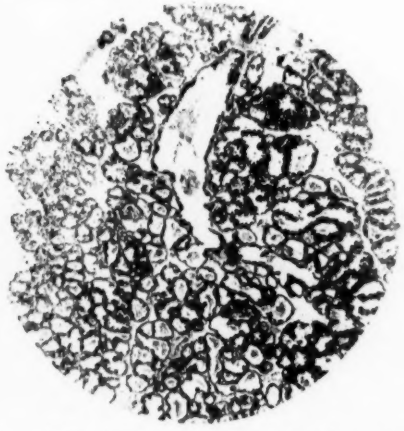

Fig. 2. Fully developed mammary gland in a normal adult female rat on the seventy-fourth day after suckling has been initiated.

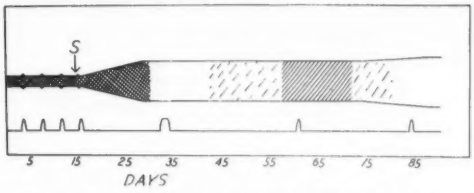


Fig. 1. Diagram showing development and secretion of the mammary gland during suckling pseudopregnancy in a rat. The upper section shows the development of the gland; the shaded parts represent the resting, the white parts the lactating condition. The line in the lower section of the diagram shows the estrus cycles.

Six of these mice were exposed to the suckling stimulus for a long time. As in the rat, these animals went into successive periods of diestrus which varied in length from 13 to 21 days (Table I).

The mammary gland changes are shown in Figures 6, 7, 8, and 9. In all cases the development seen in the rat was observed to follow the beginning of suckling. Alveoli appeared around the ducts and later secretion set in. But it is interesting to note in this connection that the secretory activity of the mammary gland showed waves during these chronic experiments.

Since the changes produced by suckling so closely resemble those of the pseudopregnancy of sterile copulation, it seemed of importance to determine whether, like the latter, they were induced by a mechanism which once initiated, would continue in the absence of the original stimulus. To do this we used 20 animals, and from them we removed the litters

Fig. 3. Enlargement of the nipple during suckling pseudopregnancy. To the left, nipple of normal adult female rat. To the right, nipple of suckling pseudopregnant rat.

Fig. 4. Left uterine horn and ovary of suckling pseudopregnant rat showing great distention of the peri-ovarian capsule.

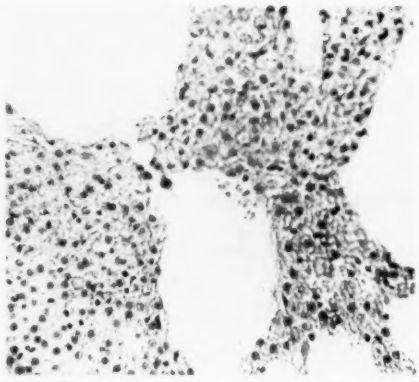

Fig. 5. Cysts in the adrenal cortex of suckling pseudopregnant rat.

at times between the fourth and tenth days of the diestrus.

In all cases, estrus appeared between the second and fifth days following the removal of the stimulus.

Some workers have reported the formation of placentomata during lactation, indicating the uterus to be progestational during this period. While we have not ourselves seen spontaneous placentomata at this time, we have been able to produce them in the mouse by scratching the interior surface of the uterus with a needle, and tying a thread at the site of irritation. We produced them in the same way during suckling pseudopregnancy (Fig. 10).

The fact that all these effects of suckling are due to changes in ovarian function is demonstrated by our observation that the mechanical stimulation of the nipple has no effect on either the uterus or mammary gland in the castrate.

## DISCUSSION

There is a striking difference between the pseudopregnancy produced by sterile copulation and that produced by suckling. In th one case the stimulation of the cervix leads t a sequence of events—enlargement of th pituitary, formation of persistent corpor lutea, development of the mammary gland inhibition of estrus, progestational develop ment of the uterus with susceptibility t placentomata formation—which is initiate by a single original stimulus. In the other the continued presence of the nervous influence appears necessary if the subsequent changes are to follow. Both bring about persistent functional corpora lutea and both result in like changes, but the modes of action seem to differ. The one may be compared to pregnancy, the other to lactation.

TABLE I

| Animal | Periods of diestrus | |
|---|---|---|
| | 1st | 2nd |
| 1 | 17 | 17 |
| 2 | 21 | 13 |
| 3 | 19 | 21 |
| 4 | 19 | 19 |
| 5 | 18 | 21 |
| 6 | 19 | killed |

This is an analogy which we would like to emphasize, and we feel that it is safe to do so in the light of our recent findings. All four conditions—pregnancy and copulation pseudopregnancy, lactation and suckling pseudopregnancy—are distinguished by corpus luteum function. In all, the uterus is in a progestational condition; in all, estrus is inhibited; in all, the mammary gland is developed. In each case the eventual appearance of estrus is inevitable: it sets in immediately at the end of normal pregnancy; it terminates the diestrus of copulation pseudopregnancy at approximately 11 days; and in both lactation and the pseudopregnancy produced by suckling in the non-lactating animal the stimulus which initiated the di estrus, however effectively maintained, i

Fig. 6. Mammary gland of a mouse taken before beginning of suckling, showing ducts only.

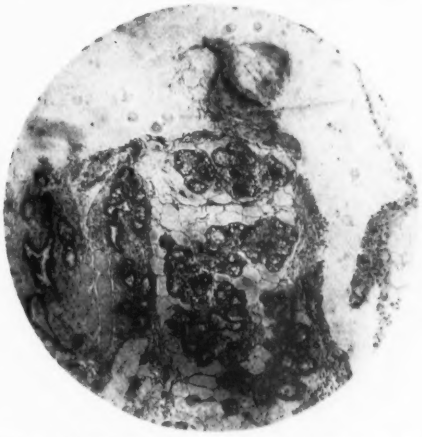

Fig. 7. Mammary gland of the same mouse taken on fourteenth day of suckling pseudopregnancy. Some alveoli have formed.

without effect on its termination. But in pregnancy and in copulation pseudopregnancy these changes are all consequent to the single original stimulus; in neither lactation nor suckling pseudopregnancy is this the case.

In suckling-pregnancy, removal of the litter led to the return of estrus; and in lactation also. In suckling pseudopregnancy, the continued application of the stimulus was necessary to mammary gland development, and involution followed almost immediately on its removal; so too with lactation.

We may conclude, then, that the diestrus of lactation is a condition produced by the stimulus of suckling, resembling in many ways that which results when the same stimulus is applied to the non-lactating animal.

While copulation pseudopregnancy apparently has no parallel in human physiology, suckling pseudopregnancy has, since the

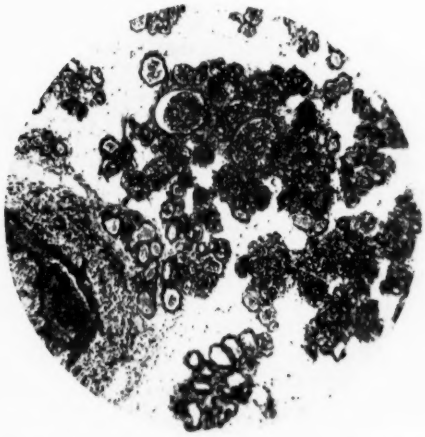

Fig. 8. Mammary gland of the same mouse on nineteenth day of suckling pseudopregnancy. Beginning of colostrum formation.

Fig. 9. Mammary gland of the same mouse on the thirty-sixth day of suckling pseudopregnancy. Full lactation.

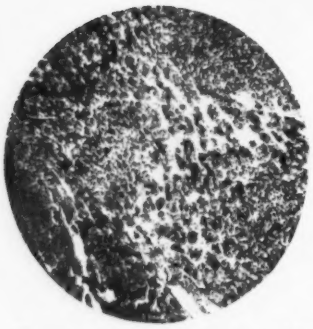

Fig. 10. Placentoma in the uterus of a suckling pseudopregnant mouse.

Fig. 11. Suckling pseudopregnant mouse nursing a litt

sexual cycles of women are inhibited during lactation. If we assume that the stimulus of nursing may produce a pseudopregnancy even in the virgin girl, then the hitherto inexplicable observations of lactation in virgins who offered their breasts to nursing infants could easily be understood. (For literature of such cases in humans, see Halban.)

## SUMMARY

It has been shown that both in the rat and in the mouse the mechanical irritation of the nipple produced by an actively suckling litter leads to full development of the mammary gland and to lactation. At the same time, long periods of diestrus appear which are interrupted by an estrus cycle only once in 2 to 3 weeks. If the nursing litter is removed from the experimental animal during the diestrus period, normal cycles reappear within a few days.

The condition which we described is very similar to pseudopregnancy produced by sterile copulation; it differs from the latter; however, in that the period of diestrus is longer and that a single nervous stimulus is sufficient for the production of copulation pseudopregnancy, while the maintenance of suckling pseudopregnancy is dependent on the continuous stimulation of the nipple, and is interrupted as soon as the nursing litter is removed.

We conclude from our findings that the interruption of sexual cyclicity during lactation is a result of the nervous stimulation of the nipple by nursing and not due to the secretory activity of the mammary gland.

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# FUNNEL PELVIS

## Its Incidence and Importance, and a New Pelvimeter for Outlet Mensuration

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A FUNNEL pelvis is one in which the measurements of the inlet are practically normal, while one or more than one of the dimensions of the outlet are smaller than normal. In general, any measurement which exhibits a decrease of 1.5 to 2 centimeters below the average may be called contracted.

It is paradoxical that the devotees of an art which is as old as the human race should have so diligently pursued the study of contraction of the pelvic inlet, and yet, until comparatively recent times, so assiduously neglected consideration of outlet contraction, or funnel pelvis.

Not until late in the eighteenth century did DuCoudray portray two cases of outlet dystocia, one representing a narrowed pubic arch, and the other a much shortened distance between the symphysis pubis and the tip of the sacrum. Twenty years later the immortal Baudelocque described an outlet which measured 7.5 centimeters between the ischial tuberosities. In 1838, Busch, in his textbook, considered the subject of outlet contraction under its own heading, and in later years the same author described dystocia in several labors complicated by this condition.

Throughout this time, however, no adequate system of mensuration was available, and the recognition of funnel pelvis was still clouded by conjecture and theory. In 1870, Breisky described a method of measuring the distance between the lower margin of the symphysis and the tip of the sacrum—a method which has survived the test of time and is still used by many obstetricians. He also described mensuration of the bisischial (transverse) diameter, thus placing the entire matter upon a more scientific basis. The introduction of this procedure accomplished much for the advancement of scientific obstetrics in Europe.

In this country we became indebted to Williams for further information concerning the pelvic outlet when, in 1909, he published his excellent monograph concerning contractions of the inferior strait which he had discovered in the course of his examinations of 1,200 women. From this series of cases Williams found that funnel pelvis not only occurs more frequently than had previously been supposed, but noted also that the condition is a not uncommon cause of dystocia. The same author subsequently continued his observations and later contributed more cases to his series. Thoms, working in the same clinic, added more to our knowledge of this subject when he published his statistics in 1915.

In general, however, a voluminous literature devotes many pages to contractions of the superior strait, while a scanty literature concerning outlet contraction appears only reluctantly to admit the latter as an obstetrical entity.

Nevertheless dystocia at the outlet may be observed when no difficulties were present at the inlet, and occasionally, when the abnormality is overlooked, an operation which promised to be a simple low forceps delivery has ended with disastrous effect upon the fetal head or upon the maternal soft parts, or upon both. The admonition of Barbour that "the fetal head is the best pelvimeter" holds true in so far as the superior strait is concerned, for here a practical application of the dictum, either manually or by a test of labor, will prove or disprove the presence of disproportion. But this test, unfortunately, cannot be applied to the outlet until late in labor, when, indeed, it may be too late if the outlet proves to be too small. And the anonymous adage, "Any head which enters the pelvis can be extracted," has its rare exceptions. At least, the head cannot always be *safely* extracted.

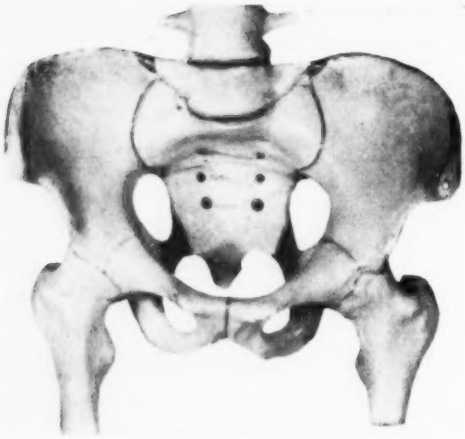


Fig. 1. Typical "high" assimilation pelvis.

One of the chief etiological factors in the production of true funnel pelvis, it is now generally agreed, lies in the formation of the so called "assimilation" pelvis. In 1900, Breus and Kolisko pointed out that the last lumbar vertebra, when fused with the sacrum, produces certain changes in the conformation of the bony canal. The sacrum, in this condition ("high" assimilation pelvis), is composed of six vertebræ instead of five (Fig. 1), while the lumbar spine is made up of but four vertebræ instead of the usual five. Frequently, as a result of this fusion, both innominate bones are rotated on a horizontal axis in such a manner as to bring their lower portions close toward the midline, thus narrowing the pubic arch and shortening the transverse (bisischial) diameter. According to various anatomists, assimilation, high or low ("low" assimilation signifying four sacral and six lumbar vertebræ, and of little obstetrical importance), is the most common of all structural pelvic abnormalities. The condition is variously reported from studies upon dried specimens, to vary from 21 to 38 per cent in frequency. The superior strait may or may not be affected by the condition,—the effect most commonly observed here being a shortening of the transverse diameter with elongation of the obstetrical conjugate.

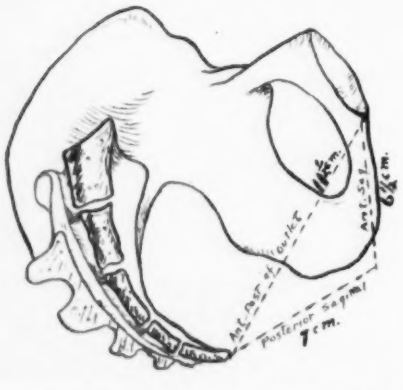


Fig. 3. Cross section of female pelvis showing relationship between the anteroposterior and the sagittal diameters.

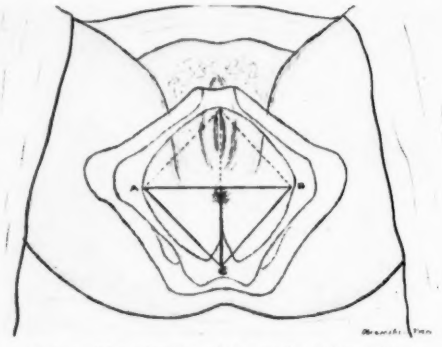


Fig. 2. The triangles of the outlet (after Klien).

Etiologically, therefore, funnel pelvis may appear as a distinct entity or may exist in the same pelvis with other anomalies which are in no way related from the standpoint of etiology.

For demonstration purposes the outlet may be said to be divided, as originally suggested by Klien, into two triangles, both of which have a common base, the bisischial diameter of the outlet (Fig. 2). This appears slightly anterior to the anus as an imaginary line, *AB*, joining the widest points of the ischial tuberosities. The apex of the anterior or urogenital triangle is the subpubic ligament, while the sides are formed by the ischiopubic rami. The posterior or rectal triangle is bounded laterally by lines from the extremities of the transverse diameter, *AB*, to the sacrococcygeal joint, which forms the apex. The boundaries of these two figures offer considerable difference, physiologically, in that the anterior

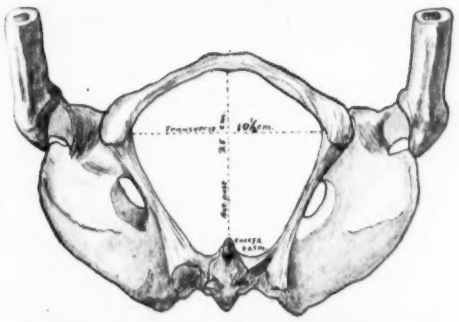


Fig. 4. The female pelvis (outlet) viewed from below.

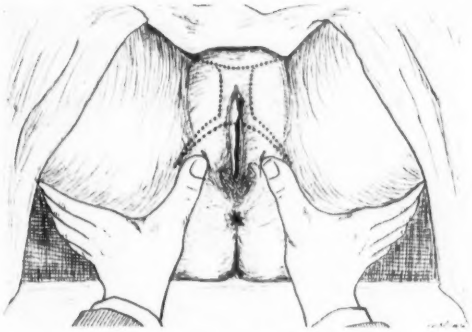


Fig. 5. Bimanual palpation of the pubic arch.

triangle possesses for its sides rigid, non-yielding bony barriers, while the sides of the posterior are soft, yielding structures, as the levator ani and the coccygeus muscles, the pelvic fasciæ, and to some extent the sacro-sciatic ligaments.

The obstetrical diameters commonly measured here are the transverse or bisischial, the anterior sagittal, the posterior sagittal, and the anteroposterior. The anterior sagittal is the imaginary line from the midpoint of the transverse (the base) to the apex of the anterior triangle, while the posterior sagittal is the measurement from the same point on the base to the apex of the posterior triangle, these measurements representing the height of the anterior and posterior triangles, respectively. The anteroposterior diameter, because of the anatomical convexity of the pudendal surface, is not the sum of the sagittal diameters, but is usually considerably less than this (Figs. 3 and 4). In addition to these observations valuable information concerning the breadth and conformation of the pubic arch can be elicited by means of bimanual palpation of the lateral rami (Fig. 5).

I have long been of the opinion that so called "normal" measurements taken from dried and often shrunken pelves are not always applicable to the living specimen, with its superadded tissue. Accordingly I studied these diameters, especially those of the outlet, with the idea of effecting a comparison. In all, 639 adult white women were measured, of which 570, or 89.21 per cent, were patients whose pelves were apparently normal. The results of these determinations are recorded as averages in Table I.

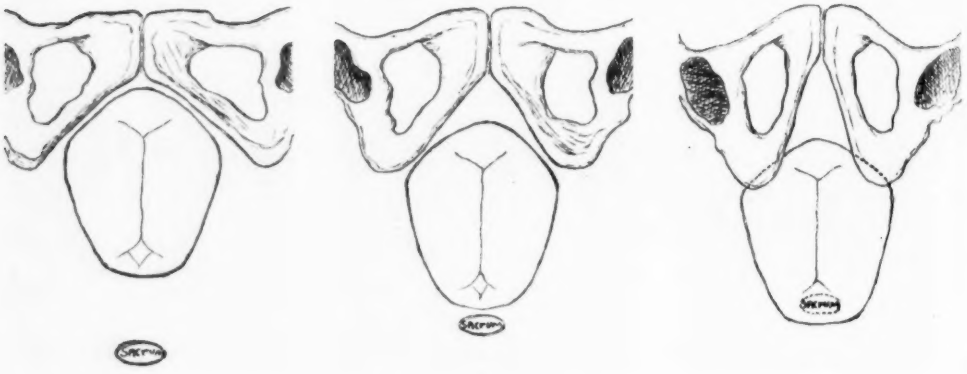
These results were compared with those of various other observers, and to secure a grand average for each diameter are grouped in Table II. It will be seen that these averages are slightly less than those commonly used in teaching.

TABLE I.—AVERAGES OF OUTLET MENSURATION IN 570 NORMAL PELVES

| Diameter | Average length, cm. |
|---|---|
| Transverse (bisischial) | 10.10 |
| Posterior sagittal | 7.70 |
| Anteroposterior | 11.32 |

TABLE II.—MEASUREMENTS OF NORMAL FEMALE OUTLET ACCORDING TO VARIOUS OBSERVERS

| Diameter | Reported by | Cases | Cm. | Grand average, cm. |
|---|---|---|---|---|
| Transverse | Williams | 185 | 10.5 | 10.01 |
| | Thoms | 1000 | 9.5 | |
| | Emmons | 217 | 9.79 | |
| | Cummings | 70 | 10.2 | |
| | Pieri | 570 | 10.1 | |
| Posterior sagittal | Williams | 185 | 7.5 | 7.75 |
| | Thoms | 1000 | 7.5 | |
| | Emmons | 217 | 7.56 | |
| | Cummings | 70 | 8.5 | |
| | Pieri | 570 | 7.70 | |
| Anteroposterior | Williams | 185 | 11.5 | 11.23 |
| | Thoms | 1000 | 10.54 | |
| | Klien | 113 | 11.5 | |
| | Cummings | 70 | 11.3 | |
| | Pieri | 570 | 11.32 | |



A. B. C.

Fig. 6. Diagrammatic representation of the head in various pelves. A, Normal outlet. B, Moderate contracti . C, Absolute contraction.

For practical purposes the normal diameters of the outlet may be taken from Table II as follows:

| | Cm. |
|---|---|
| Transverse diameter | 10.0 |
| Posterior sagittal | 7.5 |
| Anteroposterior | 11.0 |

A point of great importance concerning these measurements is that forced flexion of the thighs upon the abdomen, with the woman either upon her back or upon her side, increases the distance between the symphysis and the tip of the sacrum from 0 to 4 centimeters. The average is 1.73 centimeters (Williams).

As to the significance of the various dimensions, my experience is in accord with that of McCormick in the conclusion that there are but two practical diameters, the transverse and the posterior sagittal. The three diagrams in Figure 6 make apparent the reason for this statement, and illustrate the mechanical principle involved during labor by contraction of either or both of these measurements. Diagram A represents the normal relations of the head as it comes through an outlet of normal proportions. It will be seen that most of the available area of the anterior triangle is utilized and that no dystocia exists. In B the transverse diameter is shortened, thus lessening the available space for the head in the anterior triangle, *in spite of the increased length of the anterior sagittal diameter.* Consequently, more of the head is forced into the posterior triangle. This depicts the reason why the second stage of labor may be unduly prolonged, and illustrates the necessity for drawing the head into the posterior triangle when doing the forceps operation in these cases. It also explains the frequency of deep perineal injury which may result here from bungling attempts at delivery. The value of episiotomy in such cases, to avoid serious damage to the soft parts, is obvious. Diagram C represents the condition of absolute contraction of the outlet, which, fortunately, is rarely encountered.

Of the total number of pelves (639) measured in this series 69, or 10.79 per cent, pre

TABLE III.—FREQUENCY OF PELVIC ABNORMALITY IN 639 CASES

| White patients<br>Type of abnormality | Number | Percentage of relative incidence |
|---|---|---|
| Typical funnel | 28 | 40.58 |
| Generally contracted (justominor) | 17 | 24.64 |
| Generally contracted funnel | 3 | 4.35 |
| Flat | 20 | 28.98 |
| Naegele | 1 | 1.45 |
| Total abnormalities | 69 | 100.00 |

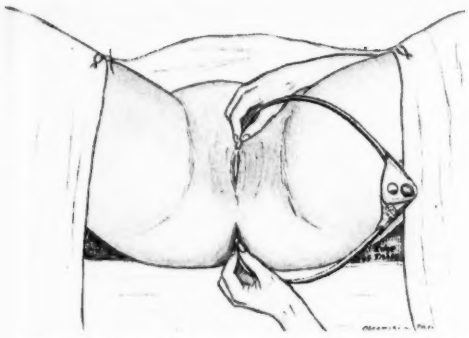


Fig. 7. Measuring the anteroposterior diameter. Breisky's method.

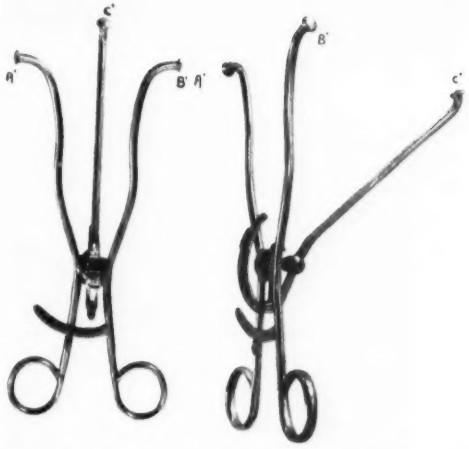



Fig. 8. The author's pelvimeter. Front and lateral views.

sented some pelvic abnormality as classified in Table III, which shows a relative incidence of funnel pelvis of 40.58 per cent. The *typical* funnel pelvis signifies a pelvis in which the abnormality of the outlet contraction exists alone. The *generally contracted* funnel pelvis signifies exaggerated outlet contraction in a pelvis already generally contracted.

For purposes of comparison the statistics of Williams and Thoms concerning white women are combined in Table IV. The incidence of funnel pelvis here, too, is seen to be greater than that of any other pelvic anomaly (36.97 per cent).

A striking similarity between my findings and those recorded by Williams and Thoms is apparent when all pelvic abnormalities are grouped under three subdivisions, namely: (1) those in which the outlet alone is contracted (typical funnel pelvis); (2) those in which the entire pelvis is contracted (generally contracted pelvis); and (3) those in which contraction of the inlet is mainly involved (practically all other types). Here again (see Table V) the incidence of funnel pelvis is seen to be higher than that of other pelvic anomalies, having been found in over 4 per cent of a total of 3,098 patients examined in the several series.

The prognosis concerning the effect upon labor of various degrees of outlet contraction is not always obvious. However, as a general rule, if the transverse is more than 8 centimeters, no difficulty need be anticipated with a head of normal size. It is frequently ob-

TABLE IV.—WILLIAMS' AND THOMS' SERIES, COMBINED, SHOWING RELATIVE FREQUENCY OF VARIOUS ABNORMALITIES IN 2,459 CASES

| White patients<br>Type of abnormality | Number | Percentage of relative incidence |
|---|---|---|
| Typical funnel | 122 | 36.97 |
| Generally contracted | 112 | 33.94 |
| Generally contracted funnel | 18 | 5.45 |
| Simple flat | 52 | 15.75 |
| Generally contracted, rachitic | 11 | 3.36 |
| Atypical | 7 | 2.12 |
| Flat rachitic | 5 | 1.51 |
| Atypical funnel | 3 | 0.90 |
| Total abnormalities | 330 | 100.00 |

TABLE V.—COMPARATIVE STATISTICS SHOWING THE FREQUENCY OF CONTRACTED OUTLET (FUNNEL PELVIS) IN BOTH SERIES OF CASES

| Type of pelvic abnormality | Thoms' and Williams' series combined 2,459 cases | | Pieri's series 639 cases | |
|---|---|---|---|---|
| | Number | Percentage of incidence in the series | Number | Percentage of incidence in the series |
| Typical funnel | 122 | 4.96 | 28 | 4.38 |
| Generally contracted | 130 | 5.29 | 20 | 3.13 |
| All other abnormalities | 78 | 3.15 | 21 | 3.28 |
| Total abnormalities | 330 | 13.40 | 69 | 10.79 |

Fig. 9. Mensuration of the outlet with the author's pelvimeter.

served, also, that although the transverse diameter is contracted, the posterior sagittal may be normal or it may even be proportionately increased, thus permitting the uneventful passage of a full term baby. According to Williams the necessary compensatory relation of these diameters is as follows:

| | Cm. | | Cm. |
|---|---|---|---|
| Transverse diameter | 8 | Posterior sagittal | 7.5 |
| Transverse diameter | 7 | Posterior sagittal | 8.0 |
| Transverse diameter | 6.5 | Posterior sagittal | 8.5 |
| Transverse diameter | 6.0 | Posterior sagittal | 9.0 |
| Transverse diameter | 5.5 | Posterior sagittal | 10.0 |

A similar study of the relation of these diameters in contracted cases is urged by J. C. Hirst, who describes the "Index of the Outlet" devised by Daniels. This index is secured by taking one-half the product of the transverse multiplied by the posterior sagittal, i.e., the area of the posterior triangle. According to Hirst this is normally $\frac{11 \times 10}{2} =$ 55 square centimeters, which is taken as the normal "Index of the Outlet." Thus, with an index of 55 to 35 spontaneous delivery is the rule; if 35 to 25, increasing difficulty may be expected; and under 25, delivery from below is likely to be impossible.

In this formula the so called normal measurements (11 cm. and 10 cm.) are larger than those found in the series detailed. I have, therefore, in making a prognosis in my cases, followed the general formula of the index mentioned, considering as normal diameters, however, a transverse of 10 centimeters and a

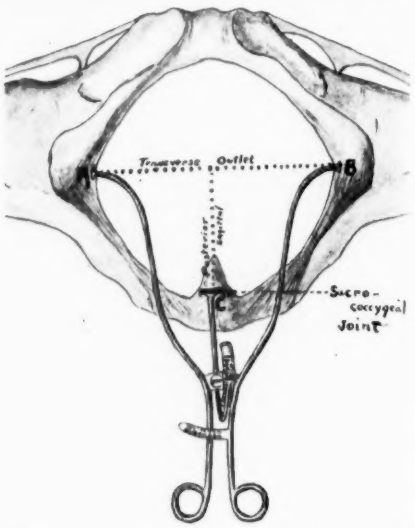



Fig. 10. Diagram to show the author's pelvimeter used upon the skeleton.

posterior sagittal of 7.5 centimeters. The normal outlet index then becomes $\frac{10 \times 7.5}{2} = 37.5$ square centimeters. With this as a basis, experience has shown that the variations of the index as tabulated below hold true for the majority of cases.

| | |
|---|---|
| Normal index of outlet, | 37.5, spontaneous. |
| Index from normal to | 30.0, forceps occasionally |
| Index from 30 to | 22.0, usually forceps |
| Index 22 or less | practically obstructive. |

It is well, however, to bear in mind that no mathematical guide should be observed too dogmatically, inasmuch as there exists in obstetrics no mathematical criterion by which we can predict the natural forces of labor, the position, the size of the baby's head, and its disposition to mold. Nor can we always foresee the surprising effect which is sometimes observed when the patient is placed in the exaggerated lithotomy position commonly used during delivery. As a result of the increase in the distance between the symphysis and the sacral tip, which this attitude often produces, a simple extraction or even a spontaneous delivery may terminate a labor which

earlier possessed the earmarks of serious dystocia.

The necessity, however, for a fairly accurate method of outlet pelvimetry, especially if the pubic arch is narrow, is obvious. The technique which I have adopted in ascertaining the measurements of the outlet has seemed to me highly satisfactory.

In measuring the length of the anteroposterior diameter (see Fig. 7) the method of Breisky was used, subtracting 1 centimeter from the reading obtained (the thickness of the tip of the sacrum). In patients in whom external palpation did not readily disclose the location of the sacral tip the finger was inserted into the rectum and the point demarcated externally.

For measuring the transverse and posterior sagittal diameters (see Fig. 2, the triangle *ABC*) a new instrument (Fig. 8) was devised with the co-operation of the manufacturer.[1] This pelvimeter, in my hands, has presented several advantages over various other implements which I have employed. With this instrument both diameters of the triangle, *ABC*, can be measured in one operation. No assistant is necessary. From the front the instrument resembles an ordinary calipers, the arms and the tips, *A′* and *B′*, of which are so constructed as to fit snugly against the ischial tuberosities in measuring the transverse diameter. A graduated scale on the anterior surface of the instrument records this distance in centimeters. The posterior arm of the pelvimeter (Fig. 8, lateral view) is freely movable laterally and anteroposteriorly, and the distance (the posterior sagittal diameter) of its tip, *C′*, from the imaginary line (the transverse diameter) between *A′* and *B′* is recorded on a second graduated scale, regardless of the position in which the instrument is held. This second scale is also located on the front of the instrument. When *C′* is held snugly against the tip of the sacrum (the patient's buttocks must be well over the edge of the table) with *A′* and *B′* in their respective places (Fig. 9), both the transverse and the posterior sagittal diameters can be read from the instrument at the same time. All of the points being fixed points, no shifting of the pelvimeter or of the hands is necessary during the calculation. This fact minimizes the frequency of error. In thin subjects 0.5 centimeter and in obese patients 1 centimeter is added to the reading of the transverse diameter to allow for the thickness of the soft parts, while 1 centimeter (the thickness of the sacrum) is always subtracted from the reading on the posterior sagittal scale. With a little practice the whole procedure consumes but a moment. In borderline cases, I have made it a point to take the average of three readings.

While it is beyond the scope of this paper to discuss in detail the management of labor in funnel pelvis, one is constrained to mention at least the salient indications and contraindications which arise when the condition is encountered, and which, more than anything else, bespeak here the importance of mensuration. In contraction of slight degree so simple an operation as mediolateral episiotomy alone may provide the needed additional space. This type of incision, of course, avoids the rectum. With increasing degree of contraction, early episiotomy and forceps extraction are indicated to avoid needless protraction of the second stage of labor. And in using the forceps the mechanics of the blades and the physiology of the posterior triangle (Fig. 6, *B*) should be visualized. Rupture of the symphysis, as has been reported, through the use of the blades as a lever, is an obstetrical crime.

The aftercoming head should be delivered with forceps when moderate outlet contraction exists, if, indeed it should not always be thus delivered.

Once the diagnosis of funnel pelvis is established the management of certain complications of pregnancy near term, such as toxæmia, and the hæmorrhages, becomes considerably modified, cæsarean section in these cases offering the best prognosis. During the past years in some clinics pubiotomy found favor, both because of its technical simplicity and because a permanent enlargement of the outlet is claimed for it. This procedure, however, is now so seldom elected that at the Johns Hopkins Hospital, where Williams first taught its virtues, the operation has not been performed in over a decade. The reason for

[1] The Royal Instrument Company, Box 172, Syracuse, New York.

this, of course, is largely due to the greatly improved surgical technique of abdominal delivery.

As has previously been suggested absolute contraction of the outlet is comparatively rare. When encountered the only alternative to craniotomy is an abdominal delivery.

## CONCLUSIONS

1. Funnel shaped pelvis of moderate degree is the most common pelvic abnormality in white women. It is present in over 4 per cent of all cases.

2. Any patient who exhibits narrowing of the pubic arch should be carefully scrutinized for the possible existence of this complication.

3. For practical purposes the average outlet measurements may be taken as follows:

| | Cm. |
|---|---|
| Transverse | 10.0 |
| Posterior sagittal | 7.5 |
| Anteroposterior | 11.0 |

4. The most important measurements of the inferior strait are the transverse and the posterior sagittal diameters.

5. Careful mensuration of the outlet, when any contraction exists, is of definite importance in enabling the accoucheur to formulate an opinion as to the probability of a normal or operative delivery.

6. The pelvimeter described is a simple and accurate means of determining the two most important diameters of the outlet.

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# THE STERILITY OF SURGICAL CATGUT SUTURES

## With Particular Reference to Foreign Made Catgut

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WHILE the sterility of surgical catgut manufactured in England, Germany, and America has been studied by investigators in those respective countries (1, 3, 5), no reference was found in the literature of a comprehensive study ever having been made by one investigator of the sterility of catgut manufactured in all of the principal countries of the world. Therefore, the scope of this research was made sufficiently broad to comprise a study of the sterility of practically all brands of foreign made catgut sutures, in addition to those of American manufacture. However, in view of the importance to the surgical profession of the results of my bacteriological examinations of catgut sutures sterilized with various chemical compounds, it seemed inadvisable to withhold such information until the study of all brands of sutures could be completed.

In my former paper (2) dealing with the chemical sterilization of catgut, I presented the results of the bacteriological examinations of several thousand catgut sutures which had been chemically sterilized with various strengths and combinations of twenty-seven different chemical compounds. In that investigation, which extended over a period of 2½ years, I also included a study of the sterility of 154 commercial lots comprising 1,134 catgut sutures purchased from the open market. The commercial lots embraced several American brands, together with one that was imported from Germany. Based on the results of that investigation, I pointed out the fallacy of so called "chemical sterilization" and emphasized the reliability and uniformity of carefully controlled heat sterilization for securing positive sterility of surgical sutures.

The present investigation, which is a continuation of my research work, has extended over a period of 2 years. From the open market I purchased the various brands of catgut sutures which are manufactured and sold in England, France, Germany, Japan, and Spain; and which comprise practically all brands of catgut which are marketed as sterile sutures, exclusive of those manufactured and sold in the United States of America. A total of 1,204 sutures, comprising 101 lots and 24 brands, was tested.

The sutures used in this investigation consisted of plain catgut, sizes 0, 1, 2, and 3; and chromic catgut, sizes 00, 0, 1, 2, 3, and 4. These commercial lots included eight brands of British, four brands of French, six brands of German, two brands of Japanese, and four brands of Spanish manufacture. One-half of each lot of sutures was first subjected to a careful chemical study, in order to ascertain the details of any chemical treatment to which they might have been subjected. The remainder of the lot was then tested bacteriologically in accordance with the technique previously described (2). As in the previous study, the entire suture strands—not fractional parts of them—were tested aerobically and anaerobically in tubes of sterile Novy culture medium; and all culture medium tubes were incubated 15 days.

### BRITISH MADE CATGUT

*Manufacturer A.* Repeated chemical analyses revealed the presence in these sutures of large amounts of a soluble mercury compound which was not removed by the 1 per cent sodium thiosulphate and 1 per cent sodium carbonate solution specified as a neutralizing solution in the Therapeutic Substances Regulations of 1931. This brand of catgut, when tested by the standard bacteriological method (5), had always shown entire absence of bacterial growth. Upon neutralizing and removing the large amount of mercury by means of a special neutralizing solution of 10 per cent sodium thiosulphate as a preliminary step in the standard bacteriological technique, as described in my previous paper (2), the su-

TABLE I.—BRITISH MADE CATGUT

| M'f'r | Country | Lots examined | Lots non-sterile | Per cent of non-sterile lots | No. of sutures examined |
|---|---|---|---|---|---|
| A | England | 11 | 8 | 72.7 | 126 |
| B | England | 3 | 0 | 0 | 36 |
| C | England | 7 | 2 | 28.5 | 88 |
| D | England | 7 | 1 | 14.2 | 80 |
| E | England | 6 | 2 | 33.3 | 66 |
| F | England | 6 | 0 | 0 | 68 |
| G | England | 2 | 0 | 0 | 20 |
| H | England | 2 | 0 | 0 | 20 |
| | Totals | 44 | 13 | 29.5 | 504 |

tures of 8 lots out of 11 lots examined showed an abundance of bacterial growths in the aerobic and anaerobic tubes. These growths appeared at varying intervals during the 15 day incubation period, and ranged from 48 hour growths to 12 day growths. The bacteria consisted of Gram positive non-sporulating aerobes and Gram negative sporulating aerobes; many free spores being present. Also non-sporulating anaerobes, some being Gram negative and others Gram positive.

*Manufacturer B.* These sutures contained no chemical other than chromium in the 20 day catgut; and bacteriological tests of 3 lots showed entire absence of growth.

*Manufacturer C.* Some iron and large amounts of mercury were found in the sutures. They were labeled "Sterile Catgut Plain" and "Sterile Catgut Medium-Hard"; but when a sterile solution of 10 per cent sodium thiosulphate was used as a preliminary step in the bacteriological technique, bacterial growths appeared in the aerobic and anaerobic tubes in 2 lots of the 7 lots tested; some growths appearing as early as 48 hours and others as late as 10 days. The bacteria comprised Gram positive non-sporulating aerobes and Gram positive sporulating anaerobes with gas formation in anaerobic tubes.

*Manufacturer D.* The sutures were labeled "Catgut Sterile Plain" and "Catgut Sterile 20 Day." Chemical analyses showed that iodine was present in all sutures. Bacteriological tests of these sutures by the standard method revealed the presence of Gram positive non-sporulating aerobes in 1 lot of the 7 lots examined; the growths appearing in from 48 hours up to 5 days.

*Manufacturer E.* The sutures contained a moderate amount of soluble mercury. When they were subjected to bacteriological tests by the standard method, Gram positive non-sporulating aerobic bacteria were found in 2 lots of the 6 lots tested; some growths appearing after 48 hours' incubation and others as late as the twelfth day.

*Manufacturer F.* These sutures contained a moderate amount of soluble mercury; tested by the standard bacteriological method, 6 lots showed entire absence of growth.

*Manufacturer G.* Chemical analyses showed a moderate amount of mercury present. No growths occurred when 2 lots of these sutures were tested by the standard bacteriological method.

*Manufacturer H.* There was a moderate amount of mercury in these sutures. When subjected to examination by the standard bacteriological method, the sutures of the 2 lots tested showed entire absence of growth.

*Summary.* Thus, out of eight different brands of British made catgut sutures examined, the products of four manufacturers were found to be non-sterile. Of the 44 lots comprising 504 sutures tested, 13 lots showed the presence of living bacteria; or 29.5 per cent of the lots were non-sterile (see Table I).

FRENCH MADE CATGUT

*Manufacturer I.* Chemical analyses showed a moderate amount of mercury present. When tested by the standard bacteriological method, living bacteria consisting of Gram positive non-sporulating aerobes were found in 2 lots tested; some growths appearing after 48 hours' incubation, others on twelfth day.

*Manufacturer J.* These sutures contained large amounts of iron but no other chemical. Bacteriological examination of 6 lots of these sutures by the standard method showed entire absence of growth.

*Manufacturer K.* The sutures were found to be impregnated with a soluble mercury compound. Entire absence of bacterial growth resulted when 5 lots of this manufacturer's sutures were subjected to the standard bacteriological test.

TABLE II.—FRENCH MADE CATGUT

| M'f'r | Country | Lots examined | Lots non-sterile | Per cent of non-sterile lots | No. of sutures examined |
|---|---|---|---|---|---|
| I | France | 2 | 2 | 100 | 24 |
| J | France | 6 | 0 | 0 | 72 |
| K | France | 5 | 0 | 0 | 48 |
| L | France | 2 | 0 | 0 | 24 |
| | Totals | 15 | 2 | 13.3 | 168 |

*Manufacturer L.* A moderate amount of mercury in the large sizes but none in the small sizes of these sutures was found. Bacteriological tests of 2 lots by the standard method resulted in entire absence of bacterial growth.

*Summary.* Of the four brands of French made catgut sutures examined, one brand proved to be non-sterile. Of the 15 lots consisting of 168 French sutures tested, 2 lots showed the presence of living bacteria; or 13.3 per cent of the lots examined were non-sterile (Table II).

GERMAN MADE CATGUT

*Manufacturer M.* Etched on the tubes of these catgut sutures were the words "Sterile Plain Catgut" and "Sterile Chromic Catgut 20 Day." Chemical analyses of the small size sutures showed the presence of iron but no mercury. When the sutures of 10 lots of this manufacturer were tested bacteriologically by the standard method, bacterial growths occurred in every lot; the bacteria consisting of Gram positive non-sporulating aerobes and anaerobes. Some growths appeared on the second day, some on third, some on fourth, some on fifth, and others on twelfth day.

*Manufacturer N.* Chemical analyses failed to show any chemical in these sutures. Bacteriological tests of 2 lots by the standard method resulted in entire absence of growth.

*Manufacturer O.* The sutures contained a moderate amount of mercury. Bacteriological tests of 2 lots by the standard method showed the presence of living bacteria in every suture, both the plain and chromic varieties, on the second day of incubation. The bacteria consisted of Gram positive and Gram negative non-sporulating aerobes, and Gram positive sporulating anaerobes with subterminal spores and gas formation.

TABLE III.—GERMAN MADE CATGUT

| M'f'r | Country | Lots examined | Lots non-sterile | Per cent of non-sterile lots | No. of sutures examined |
|---|---|---|---|---|---|
| M | Germany | 10 | 10 | 100 | 116 |
| N | Germany | 2 | 0 | 0 | 24 |
| O | Germany | 2 | 2 | 100 | 24 |
| P | Germany | 3 | 3 | 100 | 36 |
| Q | Germany | 2 | 1 | 50 | 18 |
| R | Germany | 2 | 2 | 100 | 24 |
| | Totals | 21 | 18 | 85.7 | 242 |

*Manufacturer P.* Three lots of sutures were subjected to chemical analyses, and large quantities of copper salts were found. One lot contained 2.62 per cent; another 3 per cent; and the third lot contained 3.30 per cent copper. After aseptically removing the copper salts from the sutures by means of the special neutralizing solution of ammonium chloride and ammonium hydroxide, described in my former paper (2), the standard bacteriological test was applied. These tests showed an abundance of bacterial growths in every lot of this manufacturer's sutures; the bacteria comprising Gram positive non-sporulating aerobes and Gram positive sporulating anaerobes with gas formation. Some growths appeared on the second day; some on the ninth day; others on the eleventh day; and some as late as the twelfth day of incubation.

*Manufacturer Q.* Chemical analyses revealed a moderate amount of mercury. Bacteriological tests by the standard method showed the presence, on the twelfth day, of Gram positive and Gram negative non-sporulating aerobes in one lot, while the other lot showed entire absence of growth.

*Manufacturer R.* The sutures contained small amounts of mercury. When bacteriological tests by the standard technique were applied, the presence of Gram positive non-sporulating aerobes and anaerobes was revealed in 2 lots; some bacterial growths appearing on second day, others on fourth, and still others on sixth day of incubation.

*Summary.* Of the six brands of German made catgut sutures, five brands were found to be non-sterile. Of the 21 lots consisting of 242 sutures tested, 18 lots showed the pres-

TABLE IV.—JAPANESE MADE CATGUT

| M'f'r | Country | Lots examined | Lots non-sterile | Per cent of non-sterile lots | No. of sutures examined |
|---|---|---|---|---|---|
| S | Japan | 1 | 1 | 100 | 8 |
| T | Japan | 1 | 1 | 100 | 8 |
| | Totals | 2 | 2 | 100 | 16 |

TABLE V.—SPANISH MADE CATGUT

| M'f'r | Country | Lots examined | Lots non-sterile | Per cent of non-sterile lots | No. of sutures examined |
|---|---|---|---|---|---|
| U | Spain | 6 | 6 | 100 | 120 |
| V | Spain | 5 | 0 | 0 | 60 |
| W | Spain | 4 | 2 | 50 | 46 |
| X | Spain | 4 | 4 | 100 | 48 |
| | Totals | 19 | 12 | 63.1 | 274 |

ence of living bacteria; or 85.7 per cent of the lots examined were non-sterile (Table III).

In conformity with these findings are the results of the 3 year study of the sterility of catgut by Konrich and Zeissler who found that 1,450 out of 2,670 (54.3 per cent) small packages of German sutures, and 584 out of 724 (80.7 per cent) large packages of German sutures contained living bacteria. Moreover, these authors state: "The larger German factories predominantly employ the dried intestines of Spanish, English, or Argentine sheep." Bacteriological examinations by Piening of 20 specimens of dried sheep intestines from Spain, England, and Argentina revealed the presence of 13 different species of sporulating anaerobes, including Clostridium welchii, Clostridium œdematis maligni, Clostridium histolyticum, Clostridium sporogenes, Clostridium bifermentans, and Clostridium multifermentans. Moreover, every one of the 20 specimens of dried sheep intestines which he examined contained sporulating anaerobes.

JAPANESE MADE CATGUT

*Manufacturer S.* Chemical analyses of these sutures were productive of little information other than that the sutures contained mercury in moderate amount. The bacteriological examination of one lot by the standard method showed the presence of living bacteria in every suture; the growths consisting of Gram positive non-sporulating aerobes and anaerobes which appeared on the second and fifth days.

*Manufacturer T.* The sutures contained a moderate amount of mercury. When one lot of these sutures was tested bacteriologically by the standard method, the presence of living bacteria was found in every suture on the fifth day of incubation; the micro-organisms consisting of Gram negative non-sporulating aerobes and Gram positive non-sporulating anaerobes.

*Summary.* The two brands of Japanese made sutures proved to be non-sterile. Two lots consisting of 16 sutures were tested, and every one of the sutures showed the presence of living bacteria; or 100 per cent of the sutures were non-sterile (see Table IV).

SPANISH MADE CATGUT

*Manufacturer U.* Chemical analyses showed these sutures to be impregnated with mercurochrome. When 6 lots were tested bacteriologically, with 10 per cent sodium thiosulphate solution as a preliminary step in the standard technique, living bacteria of the aerobic and anaerobic types were found in every lot; some growths appearing on the fourth, some on the seventh, and others on ninth day of incubation. The bacteria were Gram positive sporulating anaerobes with free spores and gas formation.

*Manufacturer V.* No chemical was found in the sutures. Examination of 5 lots by the standard bacteriological method showed entire absence of bacterial growth.

*Manufacturer W.* These sutures contained a moderate amount of mercury. When 4 lots were tested bacteriologically by the standard method, entire absence of bacterial growth resulted in 2 lots; while living bacteria were found in the sutures of the other 2 lots. The bacteria consisted of Gram positive non-sporulating aerobes and anaerobes; some of the growths appearing on the third day and others as late as the twelfth day of incubation.

*Manufacturer X.* Chemical analyses of the sutures revealed a small amount of iron in the chromic variety. When 4 lots of this manufacturer's sutures were subjected to bacterio-

logical tests by the standard method, they were found to be non-sterile. Living bacteria, consisting of Gram positive non-sporulating aerobes, together with Gram positive sporulating anaerobes with free spores and gas formation, were found in every lot on the second day of incubation. The tube labels, box labels, and circular bore the statement, "sterilized at 160 degrees"; although no mention was made as to whether the temperature referred to was based on the Fahrenheit or on the Centigrade scale. The fact that living bacteria were found in every lot is conclusive evidence that the sutures had never been subjected to heat at a temperature of 160 degrees Centigrade.

*Summary.* Of the four brands of Spanish made catgut sutures examined, two brands proved to be non-sterile. Of the 19 lots consisting of 274 sutures tested, 12 lots were found to be non-sterile; or 63.1 per cent of the lots examined were non-sterile (see Table V).

## SUMMARY AND CONCLUSIONS

1. As indicated in Table VI, 1,204 sutures comprising 101 lots of 24 different brands of surgical catgut manufactured and sold in England, France, Germany, Japan, and Spain were subjected to chemical and bacteriological examination.

2. Twenty-four brands of foreign made catgut sutures were examined during the course of this investigation. Of these, 15 brands contained living bacteria; or 62.5 per cent of the brands of foreign made catgut sutures were non-sterile. These non-sterile brands included the sutures of 4 British manufacturers, 1 French manufacturer, 5 German manufacturers, 2 Japanese manufacturers, and 3 Spanish manufacturers.

3. Of the 101 lots comprising 1,204 sutures examined in accordance with the technique previously described (2), 47 lots contained living bacteria. In other words, 46.5 per cent of the lots of sutures tested proved to be non-sterile. The bacteria found in the sutures comprised Gram positive and Gram negative non-sporulating aerobes and anaerobes; Gram negative sporulating aerobes; and Gram positive sporulating anaerobes with subterminal spores and gas formation.

TABLE VI.—SUMMARY OF RESULTS

| | |
|---|---|
| Number of brands examined | 24 |
| Number of brands found non-sterile | 15 |
| Percentage of non-sterile brands | 62.5 |
| Number of lots examined | 101 |
| Number of lots found non-sterile | 47 |
| Percentage of non-sterile lots | 46.5 |
| Total number of sutures examined | 1,204 |

4. The high percentage of non-sterile lots of foreign made catgut sutures indicates that, in their preparation, entirely inadequate heat or none whatever was used for sterilization purposes; reliance having been placed upon chemical methods of sterilization.

5. On the other hand, those brands of foreign made catgut sutures which, for the most part, showed absence of bacterial growth, possessed certain physical properties characteristic of heat sterilized catgut.

6. These results, therefore, indicate that when catgut sutures are subjected to sterilization with chemicals, or with inadequate heat, or with a combination of these two methods, there is always grave danger that the sutures will not prove uniformly sterile; thus leaving the matter of absolute sterility open to question.

7. A critical study of the results of the bacteriological examinations of these foreign made sutures serves to emphasize the importance of two conclusions set forth in my former paper (2): "*1. The so called chemical sterilization of surgical catgut by any method yet devised is inefficient and unreliable. 2. Carefully controlled heat sterilization is the only uniformly reliable and positive method of sterilizing surgical catgut sutures.*"

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# CLINICAL SURGERY

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## OPERATION FOR PHIMOSIS

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IF one is to choose between the two usual operations for phimosis, phimotomy and circumcision, he will do well to choose a third. Phimotomy, while immediately relieving the symptoms, is rather disfiguring; circumcision is also cosmetically unsatisfactory, and may be followed by a series of persisting unpleasant sequelæ.

There are a number of so called cosmetic operations for phimosis. These are more or less ingenious, and, likewise, more or less complicated, and the cosmetic, as well as the functional, results are often not entirely perfect. Even with the popular Schloffer operation, which is comparatively simple and yields good cosmetic effects, one often sees, especially at first, difficulties in drawing the prepuce back and forth, although this difficulty usually soon disappears.

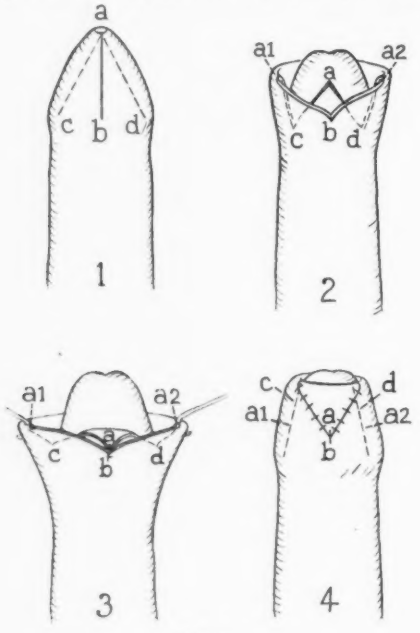


Fig. 1.

The operation which I would recommend is even more simple, and gives faultless cosmetic and functional results. The postoperative œdema subsides rapidly and even at the beginning, there are no discomforts. The procedure consists simply in making a linear incision in the outer leaf of the prepuce, and inserting a triangular flap from the inner leaf, between the edges of this incision. By this means, the outer fold of the foreskin is widened, the entire prepuce is shortened somewhat, and its opening is materially enlarged so that pulling of the foreskin forward and backward is materially facilitated.

The operation is done as follows: (1) a vertical incision is made in the dorsal midline of the outer leaf of the prepuce, beginning at the preputial orifice and extending to the region of the corona glandis, if the foreskin is short. If the foreskin is long, the incision need not be carried so far. (2) After the wound margins are separated, and the prepuce is gradually retracted and freed from the glans, a V-shaped flap is made from the inner leaf of the prepuce (Fig. 1, 1 and 2, *c*, *a*, *d*), whose apex lies at the preputial orifice, at the anterior end of the vertical incision in the external preputial fold. The base of the flap is about at the level of the proximal end of the incision in the external leaf. The two incisions in the inner fold of the prepuce, which bound the triangular flap, meet at an angle of about 70 degrees. (3) The point of the flap from the inner leaf of the foreskin, during maximal retraction of the prepuce, is united to the proximal end of the incision in the outer leaf of the prepuce with one stitch (*a* to *b*, Fig. 1, 2 and 3). With two small, sharp hooks, the wounds are drawn out lineally, and closed with continuous suture. The best material for this suture is fine catgut. The frenulum is inspected, and if necessary, divided transversely and the incision sutured in the long axis of the

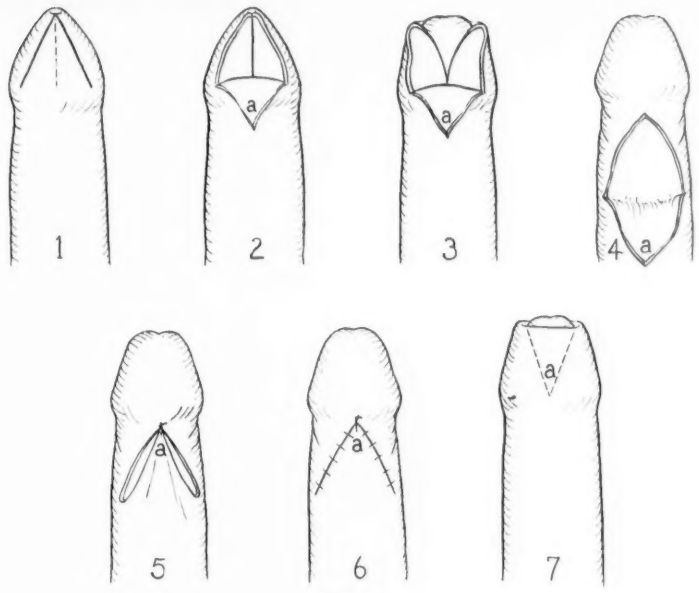


Fig. 2.

penis. (4) Restoration of the prepuce: if the flap is of proper length and breadth this should be easy (Fig. 1, 4.)

The operation is suitable for congenital as well as acquired phimoses. I usually perform it under local anæsthesia. The injection of a few cubic centimeters of novocain solution between the outer and inner leaves of the prepuce, at the site of operation, suffices for complete anæsthesia. Narcosis is necessary only in small children or in the presence of extensive adhesions between glans and inner leaf of foreskin.

The operation may also be done by inserting a triangular flap from the outer leaf of prepuce into a vertical incision in the inner preputial leaf (Fig. 2, 1 to 7). The execution of the operation in this manner is technically even easier, and it is particularly recommended when there are severe adhesions between prepuce and glans. The first described procedure, however, insertion of a flap from the inner fold of the prepuce into a vertical incision in the outer preputial leaf, seems to give better cosmetic and functional results.

Both procedures are modifications of a method which I described 25 years ago, published only in Hungarian (4). Somewhat similar techniques are reported in the German literature by Linhart and Pagenstecher. Triangular flaps of the inner and outer leaves of the prepuce are also used in the methods of Tobiasek and Druener, six flaps in the former and 4 in the latter. However, these operations are much more complicated than the one described above.

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# EXPLORATION OF THE COMMON DUCT IN GALL-STONE SURGERY

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IN the past 20 years the surgery of gall stones has changed from the relatively simple operation of incision and drainage of the gall bladder with the removal of stones to the more technical procedure of removing the gall bladder and stones. In the days of cholecystostomy the common duct was approached by the surgeon only at the rarest intervals and on the most positive indication. Improvements in technique and the advantages which present day methods in anæsthesia give have made the exposure of the common duct a much easier procedure and, therefore, its opening and inspection a more frequent undertaking. With this increasing ease of approach to the common duct there is a growing recognition of the importance of exploration of the common duct in the course of operation for the removal of gall stones.

Relatively few studies have been made of the relationship between stones in the gall bladder and stones in the bile duct. The most comprehensive study of this type with which we are familiar was made by Curtis Crump who examined the biliary tract from 1,000 consecutive autopsies (3). In this series of 1,000 cases Crump found definite evidence of gall stones in 325, or 32.5 per cent. In these 325 patients with gall stones at autopsy, 24 per cent were found to have stones in the ducts—the hepatic, common, and cystic. In a personal communication Dr. Crump informs me that if the stones in the cystic duct were omitted 21 per cent of the gall-stone cases coming to necropsy showed stones in the main bile ducts. Wilkie (quoted by Crump) found stones in the bile ducts in 18 per cent of his operative cases of gall stones. We have previously reported finding, in recent years, common duct stones in 18 per cent and over of our gall stone operations (1, 4).

TABLE I.—EXPLORATION OF DUCTS

| Years | Total cases | Ducts explored per cent | Stones discovered and removed per cent |
|---|---|---|---|
| 1910–1926 | 619 | 15.5 | 8.4 |
| 1926–1931 | 653 | 32.4 | 14.0 |
| 1929–1930 | 137 | 35.8 | 16.1 |
| 1930–1931 | 138 | 42.5 | 21.0 |
| 1931–1933 | 207 | 43.0 | 21.7 |
| 1933–1934 | 119 | 35.2 | 17.6 |

As our interest in common duct stones has increased we have explored the common duct with increasing frequency. Table I shows that in the years 1910–1926 our exploration was done in 15.5 per cent while in 1933–1934 it was done in 35 per cent. It would thus appear that of 35 to 40 per cent of the common ducts explored during the course of an operation for gall stones 17 to 21 per cent contain stones. This figure, 21 per cent, is approximately the normal percentage of stones which we should expect to find in the duct as demonstrated by the work of Crump. In view of the fact that, in our experience, we have been able to demonstrate this number of stones, we believe that it might be well to summarize our conclusions as to the indications for opening the common duct when we are operating upon the gall bladder for stones; to review the technique of choledochostomy; and to discuss the management of common duct drainage with its complications and its end-results.

While it is readily possible to outline the indications for the opening of the common duct and the search for stones during the course of an operation for gall stones, it is becoming more and more impressed upon us that, in every case, the common duct should at least be suspected of containing stones and that exploration should be withheld only for very positive reasons.

We explore the common duct when either the history or the physical examination is suggestive of common duct stones. Attacks of gall-stone colic followed by jaundice are so indicative of some obstruction to the common duct that the duct should always be opened. However, the absence of jaundice following attacks of pain, is no indication for failing to open the common duct as we have previously shown. Thus, in the years 1931–1932 we operated upon 46 patients with common duct stones and of this number 67 per cent gave a history of jaundice after their attacks of pain or were jaundiced at the time of operation. More important, however, is the fact that 33 per cent of these patients with common duct stones had no jaundice at the time of operation nor had they any history of jaundice following their pain in the past. A similar finding was made in the series of common duct stones, which we reported in

1930, in which 39 per cent of 74 patients with common duct stones had no history of jaundice in the past and were not jaundiced at the time of operation (1).

It is apparent then that we must rely very largely upon the operative findings to determine whether or not we shall open the common duct when removing the gall bladder for stones. If we find a small, thick walled, contracted gall bladder, which is the type classically associated with stones in the common duct, then we feel the common duct should be opened and investigated. If stones or thickening along the common duct can be palpated with the examining finger the common duct should be opened and explored. Any thickening should be considered suspicious and exploration undertaken. It is readily recognized that a stone of small diameter lying in the ampulla of Vater may be extremely difficult to palpate through the layers of the pancreas, the duodenum, and mesenteric tissues overlying the ampulla. Definite thickening and induration in the head of the pancreas, therefore, should lead us to investigate the common duct.

A gall bladder which contains numerous very small stones of a type which could easily pass through the cystic duct may have had stones pass into the common duct and, therefore, we open the common duct in such a case. The presence of one or two tiny stones, which can be palpated in the valves of the cystic duct, is strongly suggestive of possible stones in the common duct, and we have been impressed with the frequency with which stones are found in the common duct in this circumstance. We have noted that stones may be overlooked in the stump of the cystic duct, which is left in the dissection for cholecystectomy. We have had this experience and have reported (2) in several patients the finding of tiny stones embedded in the valves of the cystic duct which, following cholecystectomy, gave rise to recurrent attacks of biliary colic. From this point, furthermore, these stones may readily enter the common duct at a later date and give rise to common duct stones.

The operation of choledochostomy has long been considered a very delicate technical procedure which adds a considerable increment of risk and time to the operation of cholecystectomy. With recent improvements in anæsthesia, however, and with certain principles of exposure, these factors may be materially reduced and we believe that choledochostomy in the average patient does not seriously increase the morbidity or mortality of cholecystectomy. Adequate exposure of the common duct is the first consideration and adequate exposure can be obtained only by satisfactory anæsthesia. Anæsthesia which does not give relaxation of the rectus muscle, which does not prevent straining and bulging of the abdominal contents through the incision is not adequate anæsthesia for cholecystectomy. The best anæsthesia, from the surgeon's point of view, for relaxation and exposure is spinal anæsthesia. In patients, however, whose condition is not satisfactory for high abdominal spinal anæsthesia, we have found that the use of intratracheal ethylene oxygen anæsthesia combined with regional blocking of the area about the wound with one-half of one per cent novocain gives a most satisfactory relaxation and opportunity for exposure of the bile ducts.

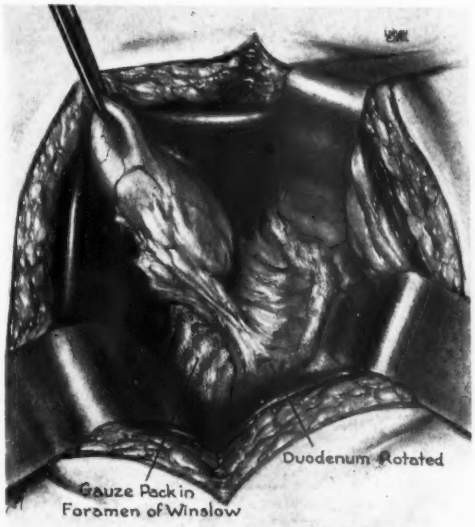


Fig. 1. Exposure of the gall bladder and the common duct area. Note the walling off of Morison's pouch by gauze packing. Note the Deaver retractor laid over gauze which is rotating the second portion of the duodenum downward and toward the midline, thus bringing out the region of the common duct.

Next in importance to anæsthesia in the exposure of the common duct is an adequate incision. This incision, we believe, should run from the costal margin, just a little to the right of the midline, down to the level of the umbilicus or below. We find no objection to a long incision provided its closure is carefully made—we are satisfied that its length is of great importance in the thorough exposure of the common duct.

With a long incision, under satisfactory anæsthesia, exposure of the common duct is dependent

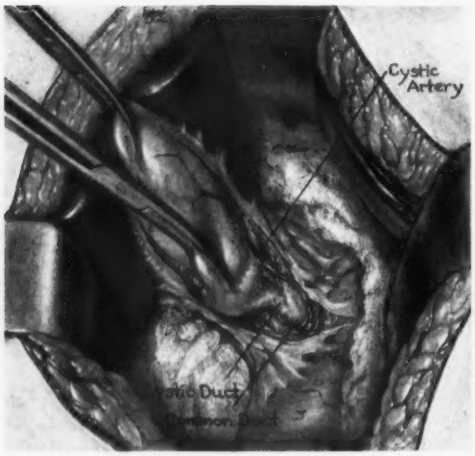


Fig. 2. With traction on the gall bladder, incisions are made in the peritoneal coat starting over the common duct and running up each side of the gall bladder. The cystic artery can be seen restricting complete extension of the cystic duct. The common duct and common hepatic duct are coming into view.

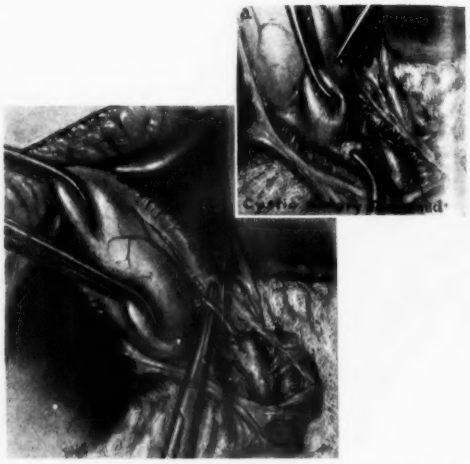

Fig. 3. The cystic artery is carefully separated a l ligated. This procedure liberates the cystic duct and mal s it readily separable from the common hepatic duct. \ small pledget of gauze on the right angle snap used as a wiper aids greatly in this delicate dissection.

upon the placing of wet packs above and to the right side of the duodenum and the use of a Deaver retractor which rotates the duodenum downward and toward the midline (Fig. 1). With forceps applied to the gall bladder for upward traction and with downward and inward traction upon the duodenum, the tissue in the gastrohepatic omentum is put upon a stretch and the common duct is at once visible in its fold.

The first step in increasing this exposure is to incise the peritoneal covering over the common duct, free it with a small wiper made of gauze and placed on the end of a clamp. The cystic duct and the cystic artery are thus demonstrated (Fig. 2). Ligature and division of the cystic artery at this time will increase the exposure of the common duct very definitely because this permits the gall bladder to be pulled upward to mark out the cystic duct and its relation to the common duct as Lahey has shown (Fig. 3). The next step in the procedure is to dissect the cystic and common ducts with the small gauze wiper so that the junction of the cystic duct with the common duct is clearly and plainly visible. At this time in the dissection the common duct, the common hepatic duct, and the cystic duct should all be directly and freely in view (Fig. 3a). It is our custom to clamp the cystic duct with two right angle clamps, leaving an adequate amount of cystic duct so that the tie will in no way impinge upon the caliber of the common duct. With a clamp, the gall bladder can be lifted up and, with retraction by the Deaver retractor, the common duct is made clearly visible.

Incision is now made in the common duct. We make this incision with a very fine pointed knife just below the junction of the common and hepatic ducts with the cystic duct. The wall of the common duct must be carefully inspected before it is incised in order to be certain that no large vessels are present (Fig. 4). If vessels are directly over the point of election for this incision, then, with fine pointed snaps, these are caught very delicately and tied. Failure to do this gives a field which is at once covered with blood when the incision in the duct is made and does not permit clear vision on opening the duct. Immediately the incision in the wall of the duct is made any bile which flows out is removed by a blunt pointed suction tube. The sides of the incision are caught by a long-handled Allis forceps, of delicate design, which permits the opening in the duct to be held widely apart. The opening in the duct may now be increased in length if it is necessary, up to 1.5 or 2 centimeters.

With the common duct widely opened before us, with the suction apparatus removing any blood and bile drainage from the duct, we explore the common duct and the common hepatic duct to be certain as to the presence or absence of stones or

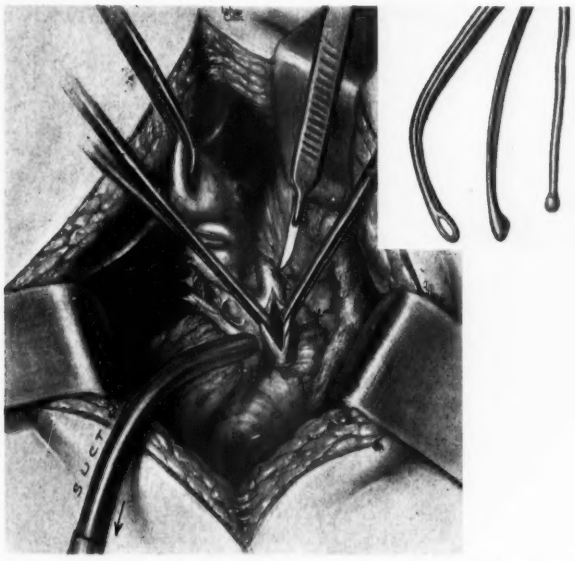


Fig. 4. An incision is made in the common duct and detritus removed by suction tube. The walls of the incision are held apart by long handled, thin bladed Allis forceps. In the insert are shown the right angle forceps used to explore the duct and pick up stones. Next is a bucket-shaped stone dislodger with a flexible shaft which occasionally passes by a stone and returns it on removal, and lastly, is a uterine probe which is very useful in exploring the common duct.

other obstruction. This is a delicate procedure and one in which there are numerous opportunities to overlook or fail to remove the stones for which we are searching. As yet we have no means at our command which will determine positively after exploration of the common duct that every stone has been removed. We use first a uterine probe, which we place in the duct and pass down to the papilla of the ampulla. Normally the ampulla has an opening which is smaller than the lead in a lead pencil and the probe is, of course, much larger than this. It is good policy, however, if one does not meet with much obstruction, gently to force the uterine probe through into the duodenum. I am satisfied that not infrequently small stones in the ampulla are, in this way, pushed through into the duodenum. If the probe meets with considerable obstruction in the ampulla, however, it is removed and stone forceps are passed downward and opened gently to see whether or not any stones or any detritus are found. If stones are found then repeated passage of forceps of various sizes and shapes is necessary until one is certain that all stones are removed or that at least no further stones can be obtained. Again the uterine probe is passed and if the duct is apparently all clear then explorations are carried out in the common hepatic duct, in the right side and the left side, to determine whether or not any stones lie in these areas. Finally, great care must be taken to explore the stump of the cystic duct in order that no tiny stones be left in that area to pass later into the common duct and cause obstructive symptoms.

When we have satisfied ourselves that no stones or débris remain in the common duct a small catheter is passed into the common duct toward the duodenum (Fig. 5). A syringe filled with sterile salt solution is attached to it and the salt solution is washed through the duct. If this salt solution passes readily through the common duct through the paralyzed sphincter at the ampulla of Vater and balloons the duodenum we feel fairly confident that no stones remain in that duct.

A T-tube is now selected which is much smaller in diameter than the common duct, which we are exploring, and the cross bar on the T is cut down so that the total width of the cross bar is a centi-

Fig. 5. Exploration of the duct has been finished. No further stones can be detected and a soft catheter of small diameter is inserted toward the duodenum. If water flushes through this catheter through the ampula and dilates the duodenum, it is probable that no further obstruction remains in the duct. Removal of the gall bladder can now be completed in the routine way leaving a peritoneal coat to cover the liver bed.

meter, or at most a centimeter and one half. The ends of the T-tube are cut on a flare so that when it comes out it will more readily pass through the opening in the common duct. The T-tube is carefully inserted, one arm in the upper end of the common duct and the other in the lower end, and with fine chromic catgut sutures swedged on a needle so that no knot is present, the duct is closed about the T-tube with one or two sutures (Fig. 6). The peritoneal tissues are gently pulled together with interrupted sutures of plain catgut, the cholecystectomy is finished in the usual manner and a cigarette drain, or small rubber dam drain, is placed down into Morison's pouch along side of the T-tube in the common duct.

Rarely the common duct will be opened and a stone will be found in the ampulla of Vater which cannot be extricated through the opening in the upper portion of the common duct. This presents a difficult and at times a trying problem. Two ways are available for removing this stone. The first is a transduodenal choledochostomy in which an incision is made through the anterior wall of the duodenum, the ampulla of Vater is opened in the posterior duodenal wall, and the stone removed through the duodenum. This operation, we have never done in the clinic. The dangers of peritonitis, of duodenal fistula or of duodenal obstruction seem too great to make this procedure desirable except in the most unusual case. The better way, in our belief, to remove a stone from the ampulla of Vater is to incise the peritoneum along the superior and lateral wall of the duodenum and gently turn the duodenum forward. With a probe in the common duct we may now follow the common duct through the head of the pancreas down to the ampulla (Fig. 7). Much bleeding is apt to accompany the dissection of the common duct through the head of the pancreas but with patience and care this can be controlled and the common duct can be opened near the ampulla just as the duct is entering the duodenum. The amount of bleeding and difficulty in obtaining exposure of the duct at this point will vary in different people but certainly two-thirds of patients will have considerable pancreatic tissue surrounding the common duct just as it enters the duodenum which bleeds readily and makes the dissection trying and long. We feel, nevertheless, that such a dissection is safer and better than procedures which entail incision in the duodenal wall.

Certain difficulties and complications have arisen in our experiences with opening the common duct many of which have been related to our failure to make a sufficiently large abdominal incision and to the difficulties which we have had in obtaining an adequate exposure of the duct. In certain very fat patients, however, exposure of the duct may be difficult because when the duct is visible the depth of the wound is very great. Bleeding from small and large vessels overlying the common duct has occurred in our experience and may be a serious annoyance in the course of the operation. This, however, can be avoided if great care is used in the dissecting, with a pledget of gauze on a clamp, of the wall of the common duct so that the exact area for the incision is visible and so that no incision through sizable vessels in the common duct is made. One should not make the incision into the common duct near the point at which it goes under the duodenum. In this area large vessels from the gastroduodenal artery may overlie the common duct and even though they are not cut at the time of opening the common duct they may well bleed later during

the course of common duct drainage. Furthermore, there is also the possibility that the common duct drain may ulcerate through the wall of the duodenum in this area. Therefore, the incision should be made three-quarters of an inch, at least, above the point where the duct goes under the duodenum.

Failure to remove all the stones in the common duct, even when it is open and when one is exploring it, may occur. No surgeon who has opened the common duct with any frequency will deny that he has overlooked the presence of stones in the duct. Small stones, which cannot be felt with the finger and which do not give any sensation to contact with the examining probes and forceps, may occasionally be overlooked. If, however, the ampulla of Vater is well dilated and if the common duct will permit the easy flow of water from a syringe into the duodenum with the catheter placed only a short way down the duct then the duct is almost always patent.

The formation of strictures after choledochostomy is a possibility which has been mentioned as a criticism of the frequent use of this procedure. We have yet, however, with our entire experience with choledochostomies to see a patient in whom any stricture formation or any evidence of stricture formation has occurred. The incision, of course, is always made in the longitudinal line of the common duct and never transversely. In the ordinary patient the tube remains in the duct only 10 to 14 days and is then removed. We are very careful not to destroy the mucous membrane of the lining of the duct because we believe that extensive destruction of this mucous membrane would tend to cause stricture formation; nor do we use such large T-tubes that mucous membrane will be ulcerated by their pressure.

The postoperative management of the patient who has had a common duct exploration and who has a T-tube in the common duct is, as a rule, not complicated. In those patients in whom the common duct is drained although no stones are found, we leave the T-tube in place for 8 to 12 days. On the sixth or seventh day after operation, the T-tube is clamped so that bile goes through the horizontal section of the tube into the intestine. If the stools become brown and if clamping the tube causes no distress and no drainage of bile around it then, after it has been clamped off for some 3 days, it is removed on the tenth or twelfth day. The sinus left by its removal rapidly heals, bile rarely drains for over 24 hours, and no further trouble occurs.

In patients in whom stones have been found and in whom there is some infection in the common duct the T-tube is left in for a longer time, often 14 and 15 days. At about the tenth day after operation the tube is clamped for an hour in the morning and an hour in the afternoon. If no trouble arises it is clamped for increasing intervals each day until finally a clamp is left on all the time so that all the bile goes through the horizontal portion of the tube into the duodenum. In these patients, when it is apparent that the bile is flowing freely into the duodenum the tube is removed at about the thirteenth or fourteenth day. Twice in our experience trouble has arisen because in some way the horizontal portion of the T-tube became kinked in the common duct; bile could neither go through the horizontal portion into the duodenum nor readily flow out through the vertical portion. In both of these cases, after some days, the T-tube was removed with immediate cessation of difficulty and final complete drainage of bile into the intestines. In each case, however, bile drained through the wound for some days in considerable amounts before the

Fig. 6. A T-tube with short horizontal arms has been inserted into the common duct after exploration. The common duct is closed about the T-tube after its insertion, and with interrupted sutures the peritoneal layers are pulled over the common duct around the T-tube. The bed of the gall bladder in the liver is also closed with plain catgut sutures and a rubber dam drain is inserted in Morison's pouch beside the T-tube after the gauze packing has been removed.

Fig. 7. Schematic drawing to show the incision of the parietal peritoneum over the second portion of the duodenum and the rotation of the duodenum toward the midline to permit dissection of the common duct in the retroduodenal portion and in the head of the pancreas. Removal of impacted stones in the ampulla by this method produces some bleeding from the pancreatic tissue, but is less dangerous than transduodenal choledochostomy.

complete flow went through the duct into the duodenum. In 2 cases that we have seen but had not operated upon, the T-tube had been left so long in the common duct that bile salts collected in it and caused an obstruction and jaundice. In each of these cases removal of the T-tube overcame this difficulty.

When large amounts of bile are draining through the T-tube in the first few days after operation we are careful to maintain the patient's fluid and salt balance by daily intravenous or subpectoral administrations of salt solution.

In all patients in whom the common duct has been opened and drained, it is most important that daily observations be made of the color of the stools, in order that one may be certain as to the time at which bile begins to enter the intestine and also as to the amount of bile which presumably is entering the intestine. In certain rare instances, when the T-tube is clamped off, bile will fail to go through into the intestine and will come out through the incision around the drain. This at once raises in the surgeon's mind, the disturbing question as to whether or not a stone has been overlooked in the ampulla of Vater, which prevents the normal flow of bile in the intestine or whether the obstruction is simply due to œdema and swelling incident to the operative manipulation. It is wise in these patients to leave the T-tube in the common duct for some time and then to try clamping the tube again. If after 10 or 12 days no bile enters the intestine it is an excellent plan to inject lipiodol through the T-tube and take an X-ray picture to determine whether or not the common duct is patent as shown by the presence of lipiodol in the duodenum or whether there is a definite obstruction. Only once, in our experience, have we encountered such an obstruction and this was due to the presence of a small collection of tooth-paste like material in the ampulla of Vater, which collected there after choledochostomy.

It has been our experience that choledochotomy does not increase the mortality of gall bladder surgery. There is, of course, a somewhat higher mortality in those patients with gall stones who have stones in the common duct and obstructive jaundice but that mortality we believe is in no way related to the incision and drainage of the common duct but rather to the liver damage and other physiological changes resulting from the obstructive jaundice. From 1910 to 1934 we have operated 1543 times for gall stones. In these patients we have opened and drained the common duct 434 times. There have been no strictures of the common duct after operation. There has been a mortality in all the gall-stone operations of 3.82 per cent. In those gall-stone operations in which the common duct was opened and drained the mortality has been 4.83 per cent, and in those in which it was not opened the mortality has been 3.61 per cent. The mortality of those patients in whom the gall bladder has been removed and the common duct explored in the absence of common duct stones has been 0.23 per cent.

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# FACTORS INFLUENCING THE VARIETY AND POSITION OF OCCIPITAL PRESENTATION AND THE MECHANISM OF ENGAGEMENT

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IT is commonly taught that the fetal head usually enters the pelvic inlet in one of its oblique diameters rather than in the transverse diameter on the assumption that the available transverse diameter is located midway between symphysis pubis and sacral promontory and as such is shorter than the oblique diameters. It is further claimed that the head more frequently enters in the right rather than the left oblique on the assumption that the rectum encroaches upon the space available in the left oblique and that, therefore, left occiput anterior and right occiput posterior presentations are more frequent than right occiput anterior and left occiput posterior presentations. The writer does not subscribe to the assumptions on which these contentions are based nor does he subscribe in principle to the first mentioned contention itself. It is rather his belief that the variety and position of occipital presentations depend first upon the conditions brought about by the accommodation of the fetus to the uterus and subsequently upon the interaction between fetal head and pelvic inlet.

Regarding uterofetal accommodation, we must remember that in the typical position assumed by the fetus *in utero*, the distance from the midpoint of its arched back to the most anterior extension of the small parts as they are flexed on its abdomen is greater than the width of the fetus either at the shoulder or hips. The anteroposterior diameter of the fetal body, therefore, accommodates itself to the transverse diameter of the uterus since the latter is greater than its anteroposterior diameter. On this basis then the child *in utero* would lie longitudinally with its back turned frankly to the right or left. There is furthermore a normal torsion of the uterus to the right around its long axis. Therefore, although the uterus is flattened anteroposteriorly chiefly by reason of the restraining action of the abdominal muscles, its left side tends to lie closer to the abdominal wall than its right side. When this is considered together with the fact that with the patient in the upright position the uterus inclines forward, we can see that the left side of the uterus, which is the most anterior, is also the most dependent portion. The fetal back will, therefore, automatically gravitate to occupy the left anterior side of the uterus since this part of the fetus is heavier than its anterior portion represented chiefly by the small parts. Thus in vertex presentations the fetus will usually be presented to the inlet as a left occiput anterior presentation, the head engaging in the right oblique diameter of the inlet. Therefore, although engagement in the right oblique is the most frequent, it is not due to explanations usually offered, but rather to the fact that the fetal head is more frequently presented to the inlet in that position as a result of uterofetal accommodation. In particular is it wrong to claim that the oblique diameters are selected because they are longer than the available transverse diameter of the inlet. The fallacy of this statement lies in the fact that as we have pointed out previously (1) the available transverse diameter is not located midway between symphysis and sacral promontory where it would measure but 11 centimeters, but rather 4 centimeters anterior to the promontory, where it measures 12¾ centimeters and is, therefore, as long as either oblique diameter. Proof of this fact may be obtained by recalling that when the head lies transversely in the inlet and as far back as possible, namely, in contact with the sacral promontory, its sagittal diameter will be 4 centimeters anterior to this landmark since the bitemporal diameter, 8 centimeters in length and extending forward from the point of contact with the sacrum, is bisected by the sagittal diameter. A transverse diameter measured at a point 4 centimeters anterior to the promontory will, therefore, constitute the greatest available transverse diameter of the inlet, because the longest presenting cephalic diameter can, if need be, come that far posteriorly in its effort to pass through the inlet in transverse position (Fig. 1). When uterofetal accommodation does not assume its usual form the head may be offered in any other diameter although the question of whether the head will *pass through* the inlet in the position in which it was first brought into contact with it, will, in all cases, thenceforth depend solely upon the interaction between the head and the inlet itself.

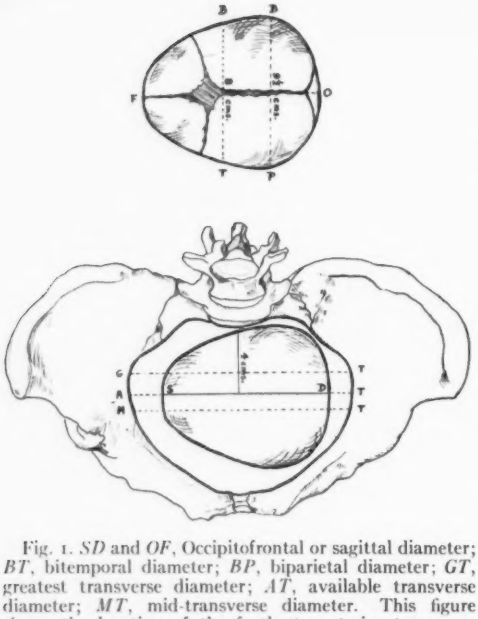

Fig. 1. *SD* and *OF*, Occipitofrontal or sagittal diameter; *BT*, bitemporal diameter; *BP*, biparietal diameter; *GT*, greatest transverse diameter; *AT*, available transverse diameter; *MT*, mid-transverse diameter. This figure shows the location of the furthest posterior transverse diameter of the pelvic inlet of which the sagittal cephalic diameter may avail itself in attempting to enter the pelvis. Such a transverse diameter is called the available transverse diameter, and it occupies the same vertical plane as the sagittal cephalic diameter which must pass through it. With the head lying transversely and as far posteriorly as possible one end of the bitemporal diameter will be in contact with the sacral promontory while the sagittal cephalic diameter which bisects the bitemporal diameter must lie 4 centimeters anterior to the promontory as must also available transverse diameter of pelvic inlet.

It will be impossible for a *normal* fetal head to pass through a normal or simple flat inlet as a left occiput posterior or right occiput posterior even if originally presented in that position. This as explained in a previous paper (2) is due to the fact that the respective sacrocotyloid diameter (the distance between the sacral promontory and anterolateral border of the inlet) is not as great as the biparietal cephalic diameter which would have to pass through it (Fig. 2). Consequently, arrest of the biparietal region takes place followed by deflection and substitution of the occipitofrontal for the suboccipitofrontal diameter as the presenting sagittal diameter of the head. As a result of this lengthening of the long axis of the presenting cephalic ovoid its frontal area will hit against the anterolateral border of the opposite margin of the inlet and will be deflected posteriorly until it lies in transverse position, in which it will then sink into the pelvis (Fig. 2). In abnormally large pelves in which, however, the normal relationship between the various diameters is preserved, the head may enter as a left occiput posterior or right occiput posterior if it is originally offered for passage in that position since in such pelves the sacrocotyloid diameter may be sufficiently large to permit the passage of the biparietal cephalic diameter. In making such engagement possible, abnormally large pelves may contribute to the occurrence of a dystocia dependent upon such engagement. If, furthermore, in association with such pelves the head is originally offered as a direct posterior occipital presentation, it may enter as such or partial rotation may occur either to the right or left oblique posterior position, in which it may enter the pelvis or from which further rotation anteriorly may occur before actual passage through the inlet. When such rotation is to the left, namely to a left occiput posterior, further rotation anteriorly is more apt to occur than when it is to the right (right occiput posterior), since it is less easy for the head to enter the inlet as a left occiput posterior than as a right occiput posterior. This is due *not* to the presence of the rectum on the left side but rather to the fact that the left oblique diameter is usually shorter than the right oblique since the majority of people tread more heavily upon their right foot, this influencing to some degree the configuration of the pelvis during the years of its growth. Thus when the left oblique is not long enough to permit ready passage of a left occiput posterior presentation, the same factors come into play to convert it into a left occiput transverse as in left occiput posterior presentations in the presence of simple flat and normal pelves (Fig. 2).

A similar chain of events may follow when an unusually small fetal head is presented for passage through a normal pelvis, as in the case of a normal head in relation to a very large pelvis. There is another rather frequent type of pelvis, namely, one in which the true conjugate is absolutely or relatively increased in relation to the transverse diameter which is actually contracted. Thoms has called attention to this type, and we ourselves have observed several cases. The inlet is irregularly oval, greater in length than width, with its posterior region slightly wider than its anterior portion. When the head is presented to such a pelvis with the occiput pointing anywhere posterior to the transverse position, it will usually rotate to the direct posterior position during the mechanism of engage-

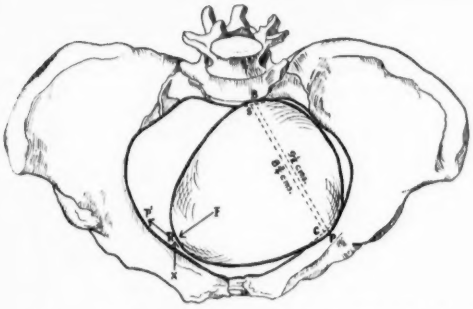

Fig. 2. *SC*, Sacrocotyloid diameter; *BP*, biparietal diameter. This figure shows that arrest occurs along the line *SC*, which is shorter than the biparietal diameter. Arrest is followed by deflection which increases the length of the anteroposterior cephalic diameter, the frontal portion of the head meeting the pelvic resistance at *R*, whence it is directed posteriorly by the counter-resistance *XR* along the line *RP*.

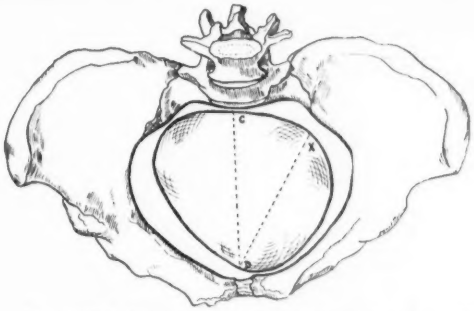

Fig. 3. This figure shows that an oblique diameter such as *DC* is longer than a transverse cephalic diameter such as *DX*. The mechanism that is brought into play when the true conjugate is shorter than the cephalic diameter *DC*, which measures about 10 centimeters and which causes rotation to the transverse position, is explained in reference No. 2.

ment, and such position will tend to persist as the head descends through the entire pelvis (3). The possibility that a deep posterior position of the occiput may be associated with such a pelvis casts doubt on the wisdom of attempting cephalic rotation with forceps to an occiput anterior position if the slightest difficulty is encountered in carrying out this procedure. It is far better to permit delivery as an occiput posterior in such cases, since here the posterior sagittal diameter of the outlet is usually also relatively large, the pelvis is relatively narrow throughout its extent, and there is less danger of injury to mother or fetus than if attempts are made at rotation.

In normal as well as in proportionately enlarged pelves, the head may enter the inlet as a left occiput anterior or right occiput anterior, but as the true conjugate becomes progressively shorter, there will be an increasing tendency for rotation to occur to the transverse position until in simple flat pelves passage through the inlet is impossible unless such rotation has occurred. This is due to the fact that when the head occupies an obliquely anterior position, the particular cephalic diameter which must pass through the true conjugate is larger than the one which is offered for passage through the true conjugate when the head is lying transversely (Fig. 3). It is in this fundamental respect that the writer's conception of the factors influencing engagement in simple flat pelves differs from that usually described (2). With equivalent degrees of shortening of the true conjugate this tendency to transverse rotation is greater in right occiput anterior than in left occiput anterior presentations due to the fact that the left oblique inlet diameter is often shorter than the right oblique.

In generally contracted pelves in which there is transverse as well as anteroposterior shortening of the inlet, the head will tend to engage in whatever particular diameter it originally approaches the inlet. The latter is irregularly round instead of oval or kidney shaped as a consequence of which, factors which otherwise might favor rotation of the head into a more suitable diameter than perhaps the one in which it was presented, are entirely absent. In such cases extreme flexion and molding are the only means which may make possible the descent of the head through the inlet.

## SUMMARY

It has been shown that the prevalence of left occiput anterior presentations is due first of all to the fact that uterofetal accommodation is such that the head is more frequently brought to the inlet in that position. Subsequently, it is due to the fact that the relationships between the various cephalic and pelvic inlet diameters are such as to maintain that position when they are normal, and to the fact that equivalent degrees of variation from the normal dimensions are less apt to alter this position than any other one. In the latter there is a marked tendency for rotation to be effected to one of the transverse positions of the occiput which then rank next in frequency to left occiput anterior presentations. It would seem that the head is able to pass through the inlet as a frank or oblique posterior occipital presentation only in generally

contracted pelves, in pelves which though large show an actual or relative transverse contraction together with an anteroposterior lengthening, and finally in unusually large pelves in which the various diameters are normally related.

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# THE TREATMENT OF VARICOSE VEINS

## Anatomical Factors of Ligation of the Great Saphenous Vein[1]

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In recent years we have been forced to return to ligation of the great saphenous vein in the treatment of certain cases of varicose veins. The injection treatment alone fails to give permanent cure in those patients in whom there is great widening of the saphenous veins. In those cases the valves are incompetent and the flow of blood in the vein is reversed: that is, it is downward from the saphenofemoral junction to the varices.[2]

Howard *et al.* first demonstrated that in such a vein there occurs recanalization of the segment sclerosed by injection. The recanalized segment may be the varix itself or the blood may course through it to re-dilate a varix below (Fig. 1). The blood may also be sufficiently diverted through a previously normal collateral to dilate it. Then the blood may flow freely through this second collateral to dilate the varix below.

We have thus come to a realization that the injection treatment is not a cure all. We must again concern ourselves with the abnormal physiology of varices, especially with the abnormal reflux from above in the severer cases. These must be treated by something more than injection alone. It is necessary to remove the baneful effect of the pressure of the refluxed blood, which breaks up the newly formed clot, or dilates the previously normal collateral. Further in this paper will be discussed the production of incompetence of the valves of previously normal collaterals (Fig. 2).

It is interesting that, in receding from our erstwhile overenthusiasm for the injection treatment, we arrive at the same procedure that Tavel, in 1904, came to, in proceeding from the purely operative view. In discussing the disappointing results from simple ligation, he observed: "My impression was also that the results were more generally favorable in those cases (after ligation) with spontaneous thrombosis than in those without; which led me to attempt an artificial thrombosis to give an even better result." He therefore carried out a preliminary ligation of the saphenous vein, and followed this, in 24 to 48 hours, by injections of 5 per cent phenol. Considering the unfavorable sclerosing agent he used, his results were very good.[3]

Schiassi in 1908, next adopted this combined treatment (20, 21). Schiassi was impressed by the value of the sclerosis to be obtained by injection. (He used a solution of iodine and potassium iodide.) He considered, however, that a preliminary ligation would give additional guarantee against any chance of embolism. Accordingly, he excised 2 or 3 centimeters of the saphena magna, above or below the knee, and injected 30 to 50 cubic centimeters of his solution into the distal segment.

Coming forward to our present era, we find Moskowicz of Vienna, reporting, in 1927, on a preliminary ligation of the saphenous vein, followed by injections of dextrose solution into

[2] The demonstration of this reversed flow is called the Trendelenburg test (24). Trendelenburg's description reads: "Lay the patient flat, lift the leg up vertically, the varices empty. Now compress the saphena magna with the finger. Stand him up quickly. The varices fill slowly, but not as much as previously. Now let the finger go, and the varices fill very quickly and fully, by a column of blood which is seen to shoot downward in the saphena magna."

This is now commonly called a *singly positive Trendelenburg test.* It denotes insufficiency of the saphenous valves.

The term *negative Trendelenburg test* refers to that result in the above experiment, in which there is no increased or rapid distention of the varices either before, or after the compressing finger is removed from the saphenous. It indicates competency of the valves of the saphenous as well as of the perforating veins connecting the deep with the superficial veins.

A *doubly positive Trendelenburg test* shows itself as a quick filling of the varices, before the release of the saphenous, as well as a downward reflux after its release. It indicates (1) incompetency of the valves of the perforating veins with a flow from the deep to the superficial veins (the reverse of normal), as well as (2) incompetence of the valves of the saphenous valves.

[3] For the sake of simplicity I use, throughout the paper, the term ligation to include preliminary section of the vein. It has been demonstrated for centuries that simple ligation of a blood vessel may allow the lumen at the ligated point to be re-established, usually by absorption of the ligature or its cutting through the vessel. If the vessel is first sectioned, however, and then ligated, this will not occur. This is, I believe, a basically conceded axiom in vascular surgery.

[1] From the Circulatory Clinic, the Boston City Hospital, and the Departments of Surgery and Anatomy, Tufts College Medical School. This study was aided by a grant from the E. P. Charlton Fund for Research in the Medical School, Tufts College.

the distal segment. His reasons for doing this are first, that percutaneous injections may give sloughing; second, that the danger of embolism is obviated by the ligation of the main trunk.[1]

DeTakats is to be credited with a return to a preliminary ligation, for the type of case under discussion (that with a positive Trendelenburg test) from a hydrodynamic viewpoint. A similar procedure has been evolved at the peripheral circulatory clinic of the Massachusetts General Hospital and reported by Faxon of that Clinic. It has, I believe, certain peculiar advantages (5). They perform the ligation at the saphenofemoral junction, and inject sclerosing solution (a mixture of invert sugar and sodium chloride) into the cut, distal segment. They also divide all the entering tributaries of the saphenous to be found at the operative level. At the Boston City Hospital, we have adopted this procedure for cases showing a positive Trendelenburg test, and we have been using it since the middle of 1932.

## HISTORY OF SAPHENOUS LIGATION

The history of saphenous ligation is literally one of upward progression (Fig. 3). Hippocrates directed the making of small punctures over the varices proper, but forbade free incisions. Celsus (1st century A.D.) made incisions along the varices at intervals of four fingers' breadth, then touched the vein in the depth of the wound with the cautery, then grasped its ends and tore out as much vein as possible.

Ætius, in the 6th century, and Paulus Æginata in the 7th century A.D., were probably the first to adopt actual section and ligation of the saphenous vein itself. The operation is fully described by Paulus and is striking in its similarity to that of modern authors. We must credit him with having recognized enough of the anatomy of the saphenous and its branches to attempt an approach on the veins sufficiently high to secure, as he thought, the main trunk from which all the branches arise. He states: "those (varices) in the leg may be operated upon in a similar manner, *making the attempt upon those in the inner part of the thighs, where they generally arise; for below this, as they are divided into many ramifications they are more difficult to succeed with.*"

The ancient surgeons that followed were apparently divided into two groups, those who operated on the leg itself, according to the method of Celsus, and those who ligated the saphenous according to Ætius and Paulus.

Coming forward to a much later date, we find Ambroise Paré (1579) ligating the saphenous just below the knee, quoting Paulus, however, for the actual technique (17). Paré states: "one attacks the varix in the upper part of the leg, a little below the knee, where most of the varices are found and take their origin. . . . One incises (first) to let out the blood and other humeurs contained in the varices, which flow to the ulcers located below on the leg, or, (second) because the vessel is so greatly distended with blood that it may break, producing the death of the person by reason of great hæmorrhage." Trendelenburg criticizes Paré for undertaking the operation with misguided notions of the circulation of the blood in the veins. Nevertheless, Paré was first a clinician, and it is not to be thought that, in those days of sepsis and no anæsthesia, any person with varices came for surgical treatment unless the disease was so far advanced that there was actually a reversed flow in the superficial veins of the leg.

For the next two centuries the operation was seemingly discarded. At the end of the 18th century appeared an excellent work on the treatment of ulcers of the legs by Everard Home, brother-in-law of John Hunter. He writes: "An enlargement of the veins produces also another effect. The coats of the vessels and the valves become thickened, which renders the valve less pliant, *they do not occupy the whole area, and therefore are no longer of any use;* and from this defect the whole length of the column of blood in the vena saphena is, in the erect position, pressing upon the contents of the smaller veins, so as to dilate them still more and more, and keep the limb always in a weak state." He proposed to take this pressure off the varices by making an "artificial valve," by ligating the saphenous at the knee.

He is later quoted by Sir Charles Bell as stating that the pressure on the varices is not only that of the blood contained in the saphenous vein, but also "the whole column of blood presses from the head and heart upon the veins of the leg!"[2] Home continues: "Cases occur in which there is

[1] Concerning sloughing at the injection site from escape of the solution to the peri-venous tissues: with reasonable care and experience, this should occur but infrequently. In our clinic at the Boston City Hospital, even a small point of necrosis is seen no more frequently than once in every hundred injections.

Concerning the production of embolism in the percutaneous injections: though an occasional embolism has been reported in the literature, our experience has been very favorable. 3,043 cases have been treated, from the inception of the circulatory clinic in 1929 to January 1, 1934. The number of injections has been approximately 20,579, yet to my knowledge, embolism has never occurred. Probably the greatest single factor of safety we possess in this clinic is the exclusively ambulatory nature of our clinic, and the active types of occupations pursued by our patients. In this way we avoid the formation of stagnation thrombi in the veins, adjacent to the area in which there has been the formation of a firmly adherent clot, secondary to chemical irritation of the intima. As DeTakats has pointed out, emboli are more apt to arise from the stagnation thrombi (2, 3).

[2] "We are indebted to Sir Everard Home for this improvement in surgery (saphenous ligation) and he has the further merit of instituting the operation from a previous careful investigation of the pathological principle." (1).

a smaller vein running parallel to the vena saphena. This, when the vena saphena has been taken up, afterward becomes enlarged, and continues the disease; when that is the case, this vein must also be taken up. These circumstances ought to be attended to in the first examination of the disease, as sometimes the two veins are so close together that they may both be included in the same ligature." One may cite with interest one of his case reports, that of Case II, Sarah Stapleton, operated on in 1794. "In the time of operation, a smaller vein was opened running parellel to the vena saphena, which afforded a reasonable suspicion that the disease might recur. . . . Fifteen months after the vena saphena had been tied, a vein in the place where the ulcer had formerly been situated burst, and bled freely. . . .

"Upon examining the vena saphena, at the part where the ligature had been applied, two very large veins were discovered; so that there must have been, at the time of the operation, two small branches, one on each side of the vena saphena; one of these only had been observed at the former examination. These two veins were now included in one ligature."

The celebrated Langenbeck apparently used the operation of saphenous ligation. A comment in 1860 on one of his cases, is interesting: "In a case of very large varices of the vena saphena in a young man, I extirpated about 3 inches (Zoll) of the dilated vein, and ligated the upper and lower ends. One year later I found a new venous trunk the width of a crow-quill, in the region of the extirpation scar, which (vein) had reconnected the well dilated ends of the saphenous."

The presence therefore of collaterals of the saphenous which could take over its flow to the varices below, was known before Trendelenburg's time. In that intervening century, too, descriptive and artistic anatomy reached a high degree of accuracy. Such works as that of Spalteholz, Tolt, Testut, Braune, picture the saphenous and its collaterals very well. Trendelenburg in his work on ligation makes specific reference to the paper of Karl Klotz. Klotz figured and described branches of the saphenous communicating freely with those of other levels, as well as actual reduplications of the main trunk by somewhat narrower collaterals.

Trendelenburg writes: "Not seldom there occurs reduplication of the stem of the saphenous in longer or shorter extent, and when both these stems are varicose, the ligation can be a success only when either both are ligated, *or the vein is seized above the doubling.*" In spite of this he proceeds to dictate: "Usually the appropriate site for both finger compression and ligation is at the junction of the lower and middle thirds of the thigh, this being the usual site of great dilatation."

In 1895, 5 years after Trendelenburg had published his paper, Georg Perthes reported his results with the operation. Of 41 cases which had been followed up, 9 patients showed recurrence. In all of these there was either a regeneration of the saphenous in the form of a single trunk or in the form of many branches. In one case, "a small packet of tissue at the ligation site was excised, and it showed many outbranchings, running downward from the dilated end of the saphenous. Most of them ended blindly, but the widest of them circled close to the ligation site, and communicated with the upper part of the dilated peripheral end of the saphenous." He concluded: "It seems that in cases in which the saphenous is not present as a solitary trunk, or shows many ramifications, it were best to perform the operation high above. The higher the main trunk is ligated, the fewer will be the number of branches above the ligation site, and the less likely will be the chance for the varices again to come under the influence of the blood's pressure. In cases of large varices spread over the entire limb, one can show that a compression right at the entrance of the saphena magna in the femoral has a definite effect on the Trendelenburg test while at all other sites there is either no effect or it disappears quickly. This is therefore preferred as the site of election for operation in these cases." Though one of his case reports (No. 41) contains this recommendation, I do not know whether he actually performed this high operation.

In 1896, a year later, Moore of Melbourne reported on a modified Trendelenburg operation. He wrote: "Site of ligature: As the operation aims at preventing any reflux of blood into the vena saphena and its branches, this object is surely much better attained by ligaturing above the junction of any of the branches belonging to the lower extremity; if the ligature is applied low in the thigh, this object is not attained with the same certainty." Though he evidently intended to operate at the fossa ovalis, he directed the making of the incision 2 inches below Poupart's ligament. Moore performed the operation in the out-patient department, applied a collodion dressing and allowed the patient to go home immediately. He reported no untoward effects.

It remained[1] for John Homans of Boston in 1916, to insist that the ideal operation for varicose veins was to ligate the saphenous and all its

[1] It is to be noted that Tavel stated that, when the varices reach the knee or thigh, the operation be done at the saphenofemoral junction (21).

terminal branches at the saphenofemoral junction, and to follow this by an excision of all the varices below (7, 8). I believe that this opinion, from the operative viewpoint, does not differ in principle from the opinion from the injection viewpoint. In other words, in either case, the ligation is done to remove the dilating effect of the back pressure of the blood, and the subsequent sclerosis of the veins below is directly comparable, in its effect, to their extirpation.

### CLINICAL

My attention has been the more directed to the correct level for ligation by patients showing recurrence of varices after improper operation. We have seen at the Boston City Hospital many such cases. I shall cite 2 case reports illustrating the recurrence after simple saphenous ligation and excision; and 2 cases showing recurrence after the present day procedure of ligation and retrograde injection of the saphenous vein.

CASE 1. F. H. (B. C. H. No. 288924), a night watchman aged 63 years, was operated on for varicosities of both extremities 15 years ago. The varicosities disappeared until 3 or 4 years before present examination. About three months before examination a large ulcer appeared on the lower anterior surface of the right leg. Examination disclosed an operative scar on the medial surface of the right lower extremity, commencing 7 inches below the pubic tubercle, then running down to within 5 inches of the medial malleolus. A second scar extended downward and forward for 8 inches from this first scar in its lower extent. A third scar of 9 inches was seen on the anterior surface of the leg. A large excavated ulcer 3 inches in diameter was situated below the terminal ends of the scars. A large group of tortuous varices, the diameters varying from 1 to 1.5 centimeters were present on the anterior, medial aspect of the leg. Above one could see and feel the stump of the saphenous vein above the long scar and from its lower extremity collaterals running on either side of the scar to feed the varices below. The Trendelenburg test was singly positive. The venous pressure in the upper part of the saphenous vein was 30 millimeters mercury rising to 40 millimeters during the Valsalva experiment. In one of the varices below the knee the pressure was 42 millimeters mercury, rising to 82 millimeters on performing the Valsalva experiment.

Here apparently was an extremity in which extensive dissection of the great saphenous vein and its varices had been done. The vasogram confirmed the gross appearance, however, of regeneration of the varices through communications with the stump of the saphenous vein (4). (Fig. 4.)

CASE 2. J. L. (B. C. H. No. 302571), a Swedish baker of 35 years, who was refused admission to this country because of large, long standing varices in his left leg. He was therefore operated upon in his native country, then allowed to enter the U. S. After being here one year, the varices returned. Examination showed varices up to 1.5 centimeters in diameter all along the medial aspect of the left leg and lower thigh. There was an operative scar along the line of the saphenous vein starting at the junction of the middle and lower thirds of the thigh and extending down to mid leg. The venogram disclosed, as in Case 1, a reformation of the varices by a downward flow through a large collateral of the saphena magna. (Fig. 5.)

CASE 3. D. G. (B. C. H. No. 211074), a restaurant worker of 34 years, had varices of both legs, the largest ones were in the right leg. The saphena magna and its branches in the right thigh and leg were widened up to 1 centimeter in diameter. The patient complained of cramping on walking and of an itching dermatitis of the lower leg. The Trendelenburg test was singly positive. He entered the Boston City Hospital on December 5, 1932, where section of the saphena magna vein was done and 15 cubic centimeters of varisol injected into the distal segment. On January 12, 1933, 5 weeks later, the patient returned to the vein clinic. He stated that his symptoms were entirely relieved. Examination showed a 2 inch transverse scar about 3 inches below the pubic tubercle. From the lower part of the scar the saphenous vein could be felt as a well sclerosed cord down to about the middle of the thigh, but from here downward it could be seen and felt to contain a good sized lumen. Running into the lateral aspect of this open part of the saphenous could be seen a dilated system of veins. Figure 6 is a composite tracing of 2 venograms made of this limb at this time. The superficial lateral femoral vein is seen to be responsible for the communication between the terminal part of the saphena magna above and the same vein below.

CASE 4. J. D., (B. C. H. No. 64763) a laborer of 53 with moderately severe diabetes of many years' duration and arthritis of both hips with partial ankylosis. Nineteen years ago he first noticed a spontaneously appearing ulcer of the left leg. In August, 1931, varices in this leg were noted and injections of quinine urethane started. In July, 1933, he had already had 43 injections with persistence of the ulcer and the appearance, meanwhile, of a smaller ulcer on the right leg. The great saphenous vein and its branches were palpable on each side in spite of the fact that they had presumably been sclerosed. The varices in the legs varied up to 1.5 centimeters in diameter. The Trendelenburg test was singly positive. Ligation and retrograde injection of both saphenous veins was carried out on July 21, 1933. One month later the saphenous veins were entirely sclerosed and the ulcers healed. The patient volunteered the information that a feeling of pressure in the legs had disappeared. In the next few months, however, the sensation of pressure and pain in the legs returned. Examination December 7, 1933, showed the presence of patent great saphenous veins from just below the end of each vertical scar. These scars started 3 inches below Poupart's ligament and continued for a distance of 3.5 inches. There was visible a dilated superficial vein lateral to the scar. Figure 7 shows the interruption of the saphenous vein in the region of the scar but a good sized stump lying above the scar with a bridging of this gap in the saphenous by a rete of lateral femoral cutaneous veins.

It happens that in 3 of these 4 cases, the lateral superficial femoral vein was responsible for bridging the gap in the saphenous vein. However, I have seen almost as many cases in which the medial superficial femoral vein, or a medially situated collateral vein was responsible.

In contradistinction to these failures quoted is a large group of cases in which patients have

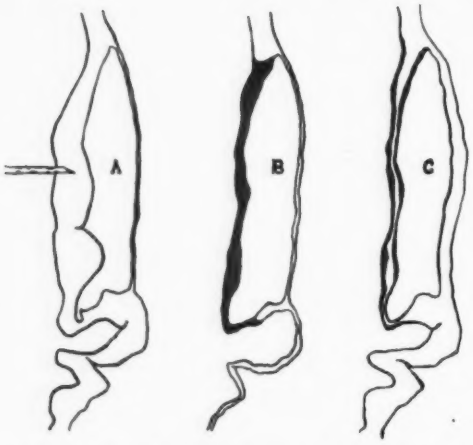


Fig. 1. The two modes of recurrence of a varix. In A, solution is being injected into the middle of a dilated venous trunk. A normal collateral also communicates with the varix below. In B, the entire dilated trunk is obliterated and the varix below is collapsed. In C, the varix has been reformed by (1) recanalization of the previously sclerosed trunk and (2) dilatation of the previously small collateral. Either or both of these two processes may occur in any given case.

been treated at the Boston City Hospital by ligation at the saphenofemoral junction with retrograde injections of the saphenous vein and subsequent injections of the varices below. We have been able in this way to obtain cures in many cases in which patients had previously had as many as 100 injections in a futile attempt to cure large varices and ulcers.

The question now presents itself: Just how high must one operate in order to be sure of securing the origins of all collaterals to the veins below? I have indicated that the accumulated evidence of the past would prove that the operation of ligation could be successful only if done *at* the saphenofemoral junction (fossa ovalis). Nevertheless, surgeons even today are placing their incisions anywhere from Poupart's ligament to the knee.

## ANATOMY[1]

Anatomical studies were carried out to ascertain at what level of the saphenous one may expect all the tributaries and collaterals finally to have ended. Dissections of fresh material as well as classroom dissection specimens were used. It was found possible to see the finer branches, the valves, and the perforating veins to the deep venous system, only in the fresh specimens.

[1] I have been assisted in the dissections cited in this section by my brother, Mr. Jesse E. Edwards, a student at Tufts College Medical School.

Figure 8 shows a diagram made from such a dissection. It illustrates the most commonly described type of superficial venous system. The vena saphena magna is seen to start as a continuation of the medial end of the dorsal venous arch of the foot. It ascends in the leg from a point anterior to the medial malleolus, to a point posterior to the medial femoral condyle, receiving many intercommunicating tributaries. These form a true collateral, posterior to main trunk.

In the thigh there are no grossly visible anastomosing tributaries above the mid thigh. The saphenous ends in the femoral vein at the fossa ovalis, the upper medial corner of which is 1.5 centimeters below and 2.5 centimeters lateral to the pubic tubercle. Here at its terminal part enter five groups of tributaries: (1) a lateral superficial femoral vein with a narrow superficial ramus and a wider deep ramus; (2) a group of medial superficial femoral veins; (3) a superficial circumflex iliac vein; (4) superficial inferior epigastric veins; (5) a superficial external pudendal vein, starting in this case as a continuation of the dorsal vein of the penis. Noteworthy is also the absence of deep communications in the thigh, and the presence in the leg of several such perforating veins in typical locations, viz.: (1) at and below the knee; (2) mid leg; (3) at the ankle and in the foot. (One of these is large and constant, accompanying the dorsalis pedis artery to the sole of the foot.) Rather typical is the presence of valves at the mouths of the perforating veins in the leg, preventing a reflux from the deep veins; in the foot the valves are either absent, or more commonly, are present and direct the blood outward.

Two communications may be seen to the vena saphena parva. This latter is atypical, starting as a perforating vein and receiving the lateral end of the dorsal venous arch only as a tributary. The saphena parva presents 2 typical perforators in its mid part, and ends in the popliteal vein, first running beneath the fascia for some extent.

The venous system shown in Figure 9 illustrates a high collateral of the saphena magna. There are two perforators in the mid and lower thigh—typical locations for their appearance. The lateral superficial femoral vein is low arising from the collateral. The vena saphena parva ends in the terminal part of the vena tibialis anterior, before the latter enters the popliteal. Before the saphena parva ends it receives, under the fascia, the vena femoropoplitea, or posterior femoral cutaneous vein, which connects it with the inferior gluteal veins. The great saphenous veins figured in Figure 10 show large collaterals

Fig. 2. Photograph of a saphenous valve in section, after its flaps had been set to prevent back flow. Note the length of the flap in contact with its fellow. This particular valve would become incompetent if the vein dilated to twice its diameter. Clinically, normal veins may dilate from three to ten times their original diameter, when put under the stress of an unusual blood flow, as in Figure 1. ×5.

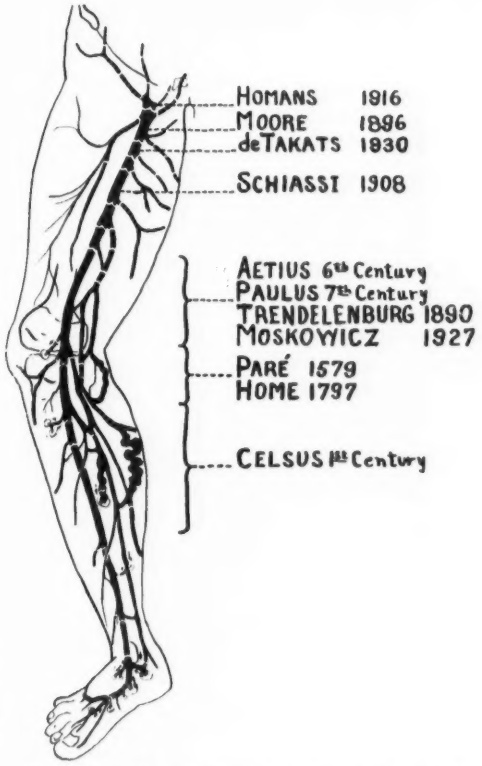


Fig. 3. The history of saphenous ligation showing the upward progression of the elective site of operation.

stretching from the saphenous high in the thigh to the same vein some distance below. They are evidently worthy of the term "reduplications" of the saphenous.

The dissecting room material was valuable for statistical data concerning, first, the actual location of entering tributaries and, second, the actual location of the fossa ovalis (Fig. 11). Thus this material enables one actually to project on the surface the position of the structures as usually encountered. Twenty-one extremities of thirty cadavers were used, the remainder being discarded because the students had dissected away the superficial structures. Attention was paid only to the terminal part of the saphenous because the previous work as quoted, had indicated that its lower portions were obviously out of the question as a site for ligation. The accompanying diagrams show the main entering tributaries of the terminal part of the saphenous and the distance of these entrances from the lower edge of the fossa ovalis indicated in centimeters. The diagrams are drawn to scale for these measurements. The fossa ovalis itself is located by measuring in centimeters the distance from the pubic tubercle to its supermedial angle, both in a vertical direction (downward) and in a horizontal (laterally).

The superficial circumflex iliac, inferior epigastric, and external pudendal veins were for the most part removed in previous dissections and are not shown in most of the diagrams except as they may enter together with the tributaries from the thigh. One or more of the three veins noted above may pierce the cribriform fascia above the saphenous and enter the femoral vein independently of, or together with, the saphenous.

From below, two rather constant veins or groups of veins are seen, the lateral and medial superficial femoral veins. The lateral is frequently the highest of these to end, entering the femoral proper above the saphenous, or the saphenous directly at its termination or the saphe-

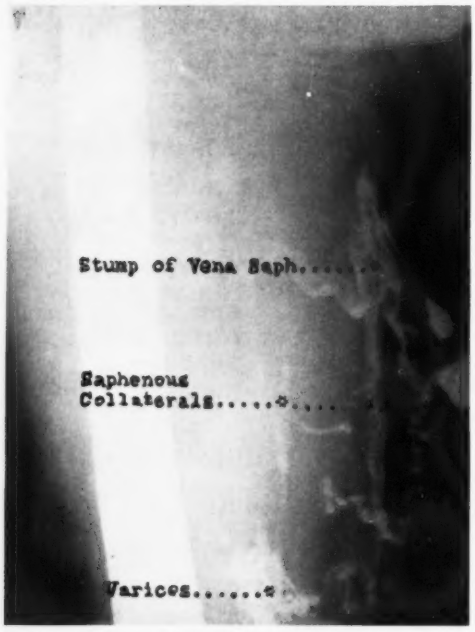


Fig. 4. Case 1. Regeneration of varices after low excision of the saphenous vein. The venogram was made with the patient standing and without the application of tourniquets. The injecting needle was thrust into the saphenous stump and 15 cubic centimeters of 40 per cent skiodan injected. Note (1) the rich anastomosis between the stump of the saphenous vein and the reformed varices below; (2) the downward flow of blood plus skiodan, i.e., a positive Trendelenburg test.

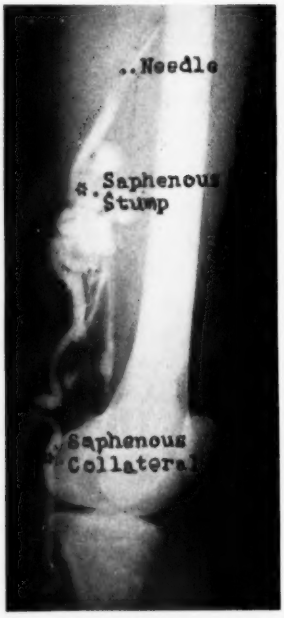


Fig. 5. Case 2. Regeneration of varices after low excision of the saphenous vein. The venogram was made with the same technique as that used in Case 1 (Fig. 4). Reprinted from the *New England J. Med.*, 1933, ccix, 1337.

nous within a few centimeters below the fossa ovalis. It sometimes receives the superficial circumflex iliac vein as it ends.

The medial superficial femoral vein usually terminates at a lower level than the lateral. It may receive the superficial external pudendal vein as it ends.

Distally, the medial superficial femoral vein may wind around the thigh, to end posteriorly by anastomosing with the inferior gluteal veins. The superficial external pudendal vein anastomoses with the deeper internal pudendal veins. Because both the inferior gluteal and internal pudendal veins are tributaries of the hypogastric (internal iliac) vein, obstruction in either the femoral or external iliac veins above the saphenous, or the hypogastric vein, may result in a dilatation of the medial superficial femoral or the external pudendal veins.

In many instances (especially in the veins figured in Figure 10) large collaterals are seen stretching between the upper and lower portions of the saphenous. Further, it becomes evident from the clinical cases that when the branches take a course near the parent trunk, the tiny intercommunications that are ordinarily insignificant, may become enlarged after interruption of the trunk below their origin so as to result in large, grossly visible reduplications of the saphenous. From my dissections I can say that the chances are unlikely that the upper three of the saphenous tributaries, i.e., the superficial external pudendal, inferior epigastric, and circumflex iliac veins, may effect any important communications with the saphenous below. An exception to this is the occasional instance when these veins terminate in common with the lateral or medial femoral cutaneous veins.

I may note here that in dissecting the region of the saphenous termination, one is struck by the fibrous consistency of the deep surface of the overlying superficial fascia. This fibrous tissue is the continuation downward of Scarpa's fascia of the abdomen. Though this fascia is adherent to the fascia lata just below the inguinal ligament, it does not end there but continue

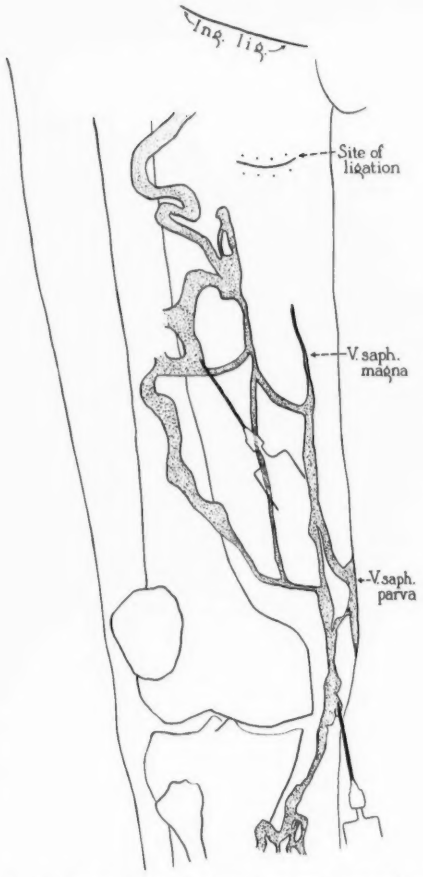


Fig. 6. Case 3. Regeneration of varices after saphenous ligation and retrograde injection of sclerosing solution. Composite tracing made from two venograms. Two separate injections were used with the patient standing up and without tourniquets. The contrast material for each injection was 10 cubic centimeters of a 20 per cent solution of sodium iodide. (I am not using this material any longer because of (1) poor contrast and (2) phlebitis following the injection.) The lateral femoral cutaneous vein is seen to be responsible for bridging the gap in the upper part of the saphenous vein.

downward to end gradually in the middle third of the thigh.

Localization of the fossa ovalis by measurement from the pubic tubercle gave the results shown in Table I.

I believe that in any case the surgeon may check his determination in the horizontal line by searching for the fossa about 1 centimeter medial to the pulsation of the femoral artery.

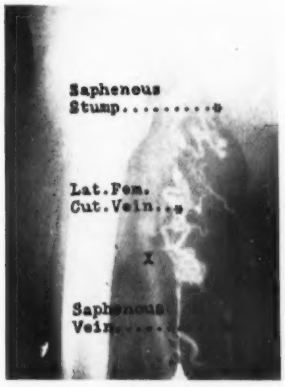


Fig. 7. Case 4. Regeneration of varices after ligation and retrograde injection of sclerosing solution. Venogram made with patient supine. Injection of 20 cubic centimeters of 35 per cent neoskiodan into the dilated lateral femoral cutaneous vein. Note (1) the lateral femoral cutaneous vein bridging the gap in the saphenous vein caused by excision of a segment; (2) the femoral vein *X*. It is indistinct because of the dilution of the neoskiodan, and also because of the movement imparted to it by the pulsations of the femoral artery.

TABLE I.

| | Horizontally | Vertically |
|---|---|---|
| Distance from pubic tubercle to upper inner angle of fossa ovalis. | | |
| Mean average | 3.9 cm. | 1.7 cm. |
| Longest distance noted | 6. cm. | 4. cm. |
| Shortest distance noted | 2. cm. | 0 cm.* |

*That is, the fossa is on the same level as the pubic tubercle.

## PRODUCTION OF INCOMPETENT VENOUS VALVES DURING TREATMENT OF VARICES

In referring to the recurrence of varices a question arises as to the ability of the normal collateral to stay normal (Fig. 1). Of course, these communications may be widened concomitantly with the main trunk or the most prominent varix. In that case, the blood will course through it unimpeded, and continue to distend the varix below, even after the main trunk has been injected. Many of these collaterals, are at first, however, of normal diameter, and well equipped with adequate valves. Through these no blood will at first be refluxed. When, however, the main trunk is interrupted by sclerosis or ligation, the entire blood mass coming down the stump of the main trunk will now be diverted into the collateral. Being of thin walls, the collateral soon begins to dilate. How much dilatation of a vein is necessary before its valve flaps cannot meet and thus become incompetent, can be answered by the following procedure.

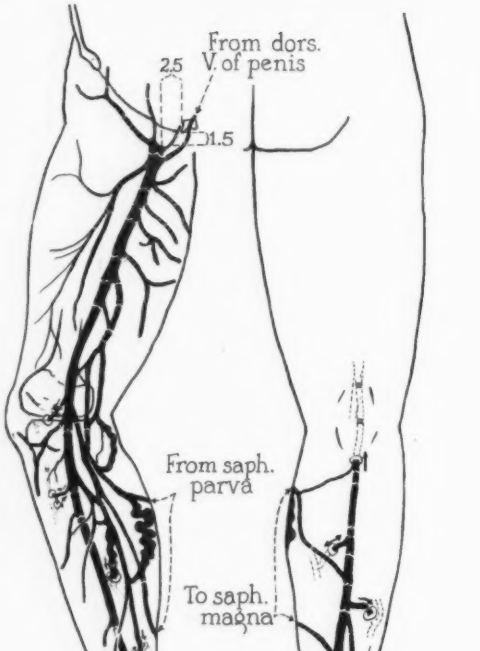


Fig. 8. Dissection of the saphenous veins: their branches, communications, and valves. The valves are indicated in white. The arrows point the direction of blood flow through a perforating vein to or from the deep veins.

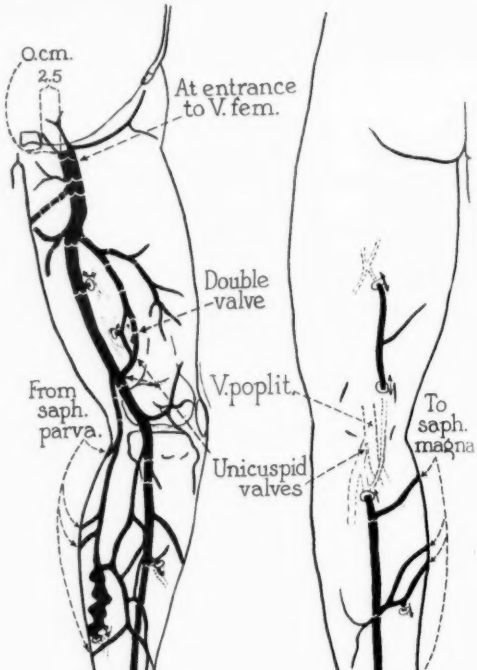


Fig. 9. Dissection of the saphenous veins: their branches, communications, and valves. The valves are indicated in white. The arrows point the direction of blood flow through a perforating vein to or from the deep veins.

Section of veins containing valves, were removed from fresh cadavers. These veins were not fixed, in order to avoid the hardening, shrinking and distortion of the delicate flaps. Each segment was hung vertically in the position it assumed in the intact body, by means of hooks. The lumen was then carefully washed with normal salt solution, then the vein segment was lowered into Delafield's hæmatoxylin solution. After the stain had acted for 2 minutes, the vein was rinsed in water and then carefully dried with absorbent cotton. A concentrated solution of gelatin was made of such consistency that it hardened almost immediately on removal from the water bath. With a pipette, this hot gelatin was dropped into the valve sinus behind each flap, thus pushing the valve flaps against each other and closing the valve. The remainder of the vein, proximal to the valve, was then filled with the gelatin. After the gelatin had hardened the vein was hung in a reversed position so that the collapsed segment, distal to the valve, could be filled with the gelatin.

The gelatin filled vein was then transferred to the freezing microtome and thick sections made longitudinally from the middle of the vein, and at right angles to the line of the flap edge. Gross photographs from these sections show the actua

mount of the flaps in contact with each other uring their setting to prevent back flow (Fig. 2). he length of flap in contact with its fellow measres generally from 0.2 to 0.5 of the diameter f the vein as measured across its center from all to wall and at right angles to the plane of he flap. Because the length of two flaps has to e taken into account the flaps will not be able o meet when a dilatation of the vein occurs quivalent to from 0.4 of the original diameter to he whole of the original diameter.

Clinically, the coming into vision of a vein hich had previously been too small to be seen, sually means a dilatation of 3 to 10 times. It ollows that at least by the time previously ormal collateral veins of small size become large nough to be seen, that their valves must have ecome incompetent, and a back flow established hrough them, to dilate the varix below.

### PECULIARITY OF VARICES OF LESSER SAPHENOUS

It has been my experience that varices of the lesser saphenous, no matter how large they may be, can be successfully obliterated by the injection treatment alone. This is in contradistinction to the large varices of the great saphenous, as previously noted. In searching for a possible reason for this difference I have been struck by a noteworthy difference in the terminations of the respective veins.

First, the saphena magna at its termination is covered only by a yielding superficial fascia, second, about one fourth of all individuals are born without any valve lying above the saphenous termination, even to the right auricle (6, 13). The dilatation of the vein involves also its terminal part as it enters the femoral. Frequently, this is so marked as to cause a good sized bulb at the fossa ovalis. In these dilated cases (such as have been under discussion as candidates for ligation) there is a very free flow into the saphenous from the femoral vein. Every sudden change in pressure as after coughing or straining is immediately imparted to the entire saphenous vein, without any considerable reduction.

When we consider the lesser saphenous vein, the termination is altogether different. First, the vein runs beneath the deep fascia for some distance before it enters the popliteal or one of the tibial veins. Lying within the unyielding cylinder of deep fascia, this portion escapes dilatation (Fig. 12). Second, the popliteal and femoral veins above the entrance to the lesser saphenous contain about six to ten valves.

In instances, therefore, of varices of the lesser saphenous sudden increases in pressure in the deep veins, occasioned as noted by coughing or straining will result in a slowly rising pressure from resistance to flow of the blood in the vena cava and heart, but the sudden downward shock of refluxed blood will be prevented. Again, the narrow undilated part of the vein will still further dampen even the slowly rising pressure by its small size and by its valves in the deep part, when they exist. This thesis is being investigated in more detail and will be reported fully later.

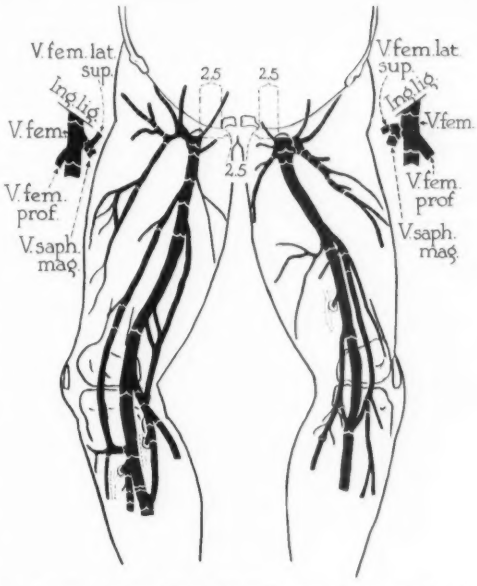


Fig. 10. Dissection of the great saphenous vein in the thigh. Valves are indicated in white. Inserts show detail of valve arrangement at the saphenofemoral junction.

### PRESENT CLINICAL CRITERIA FOR TREATMENT

I shall here briefly note our criteria for the type of treatment to be used in any given case of varices, as used at present in the Circulatory Clinic at the Boston City Hospital. I am indebted to Dr. Lawrence McCarthy of that clinic who shared with me the responsibility of arriving at the criteria.

We try to determine, at the first visit of the patient:

1. The actual presence of varices and whether they occur in the distribution of the greater or lesser saphenous.

2. The condition of the great saphenous vein and whether there is a positive Trendelenburg test.

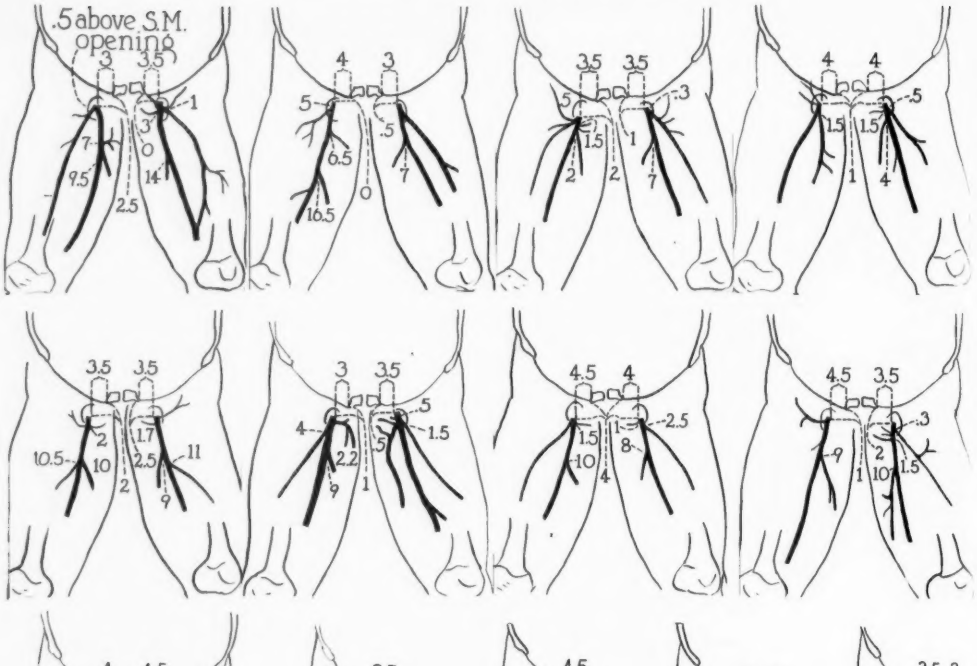


Fig. 11. Terminations of the great saphenous vein—from classroom dissections.

3. The condition of the valves of the perforating veins.

4. The condition of the deep veins.

We then proceed with our treatment:

1. If the varices are limited to the distribution of the lesser saphenous vein, we use the injection treatment alone. The solutions we use are (a) quinine urethane for the small or medium sized varices; (b) 20 per cent sodium chloride for the large varices; (c) 5 per cent sodium morrhuate for angiomata. (In private practice I prefer this solution in all cases.)

2. If the varices are in the distribution of the great saphenous vein but the vein is not widened and the Trendelenburg test is negative, we use the injection treatment alone. If the Trendelenburg test is positive, we send the patient into the hospital for ligation at the saphenofemoral junction, inject the distal segment with varisol (invert sugar and sodium chloride), then follow up in the out patient department with injections as in the cases with negative Trendelenburg tests.

3. If the Trendelenburg test is doubly positive, we ligate the saphenous, excise the incompetent perforation, and inject the remainder in the out patient department. These cases are relatively uncommon.

4. In cases of obliteration of deep veins, it is a good rule not to disturb the superficial varices. We have injected the varices in the lower leg in a case of occlusion of the inferior vena cava, with much improvement. In this case, however, the

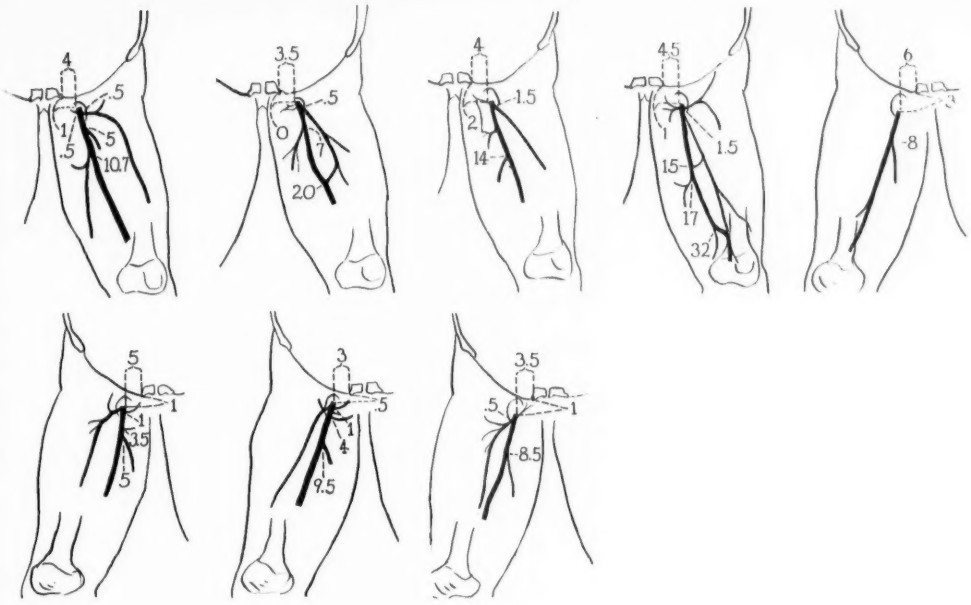


Fig. 11.

original deep phlebitis had not involved the deep veins of the leg proper.

5. Patients with ulcer we treat according to the criteria laid down above, but we inject very cautiously, staying far away from the ulcer, until it is free from infection, sometimes not injecting until we have first reduced the inflammation by ligation alone, or by supportive dressings. We have never found it necessary to excise an ulcer. If there is an incompetent perforator beneath the ulcer, we believe the ulcer can be temporarily healed by ligation and injection. The perforator can then be excised several weeks after the ulcer is healed.

6. Patients with phlebitis are treated as are patients with ulcer. The progress of the phlebitis is stopped by the ligation or small injections far from the phlebitic focus.

## SUMMARY AND CONCLUSIONS

The injection treatment alone has failed to cure permanently those cases of varicose veins with concomitant dilatation of the great saphenous vein. The failures have been due to (1) recanalization of the sclerosed segments, and, or (2) dilatation of previously existing normal collaterals.

Reports of others and our experience at the Boston City Hospital indicate so far, that a preliminary ligation of the great saphenous vein will protect the subsequently injected veins from recurrence by the above processes.

Fig. 12. Venogram of a varicosed lesser saphenous vein. The termination *t* of the vein beneath the deep fascia is well shown.

Ligation of the saphenous vein with or without subsequent injection may fail because of the reformation of the parent trunk or the varices through widening of collaterals and tributaries of the saphenous. Anatomical studies here reported, affirm the contention of Homans of 1916, that the proper site for ligation is at the saphenofemoral junction. It is only at this point that one can surely be above the origin of all the tributaries and collaterals of the saphenous vein.

The site of the saphenofemoral junction does not vary greatly in different individuals. Its average location may be found at a spot 3.9 centimeters lateral to and 1.7 centimeters below the level of the pubic tubercle. Being a bony point, the tubercle is probably the most reliable landmark for the localization of the site. On the operating table it would seem that a good rule would be to place the incision 1.7 centimeters below the level of the pubic tubercle and 1 centimeter medial to pulsation of femoral artery.

Clinical results reported from the Massachusetts General Hospital and our results at the Boston City Hospital indicate that when the ligation is carried out at the above site and all the terminal tributaries are secured, few subsequent injections are needed; the varices disappear quickly and do not recur. The cases chosen for this procedure are those with widening of the great saphenous vein and loss of valve function in that vein. Patients without this dilatation of the saphena magna are treated by injection alone.

Varices of the lesser saphenous probably never have to be treated by ligation of the parent trunk. The difference apparently lies in the fact that the lesser saphenous terminates in a fine vein running beneath the deep fascia. Here it empties into a vein which is well valved. Thus sudden rises of venous pressure traveling centrifugally are dampened and imparted but slightly, and without great momentum of the blood mass, to the surface veins.

I am greatly indebted to Dr. Timothy Leary and Dr. John Homans for helpful criticism.

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# THE ROENTGENOLOGICAL DIAGNOSIS OF MECKEL'S DIVERTICULUM[1]

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ACCORDING to Gray's *Anatomy*, "Meckel's diverticulum consists of a pouch which projects from the lower part of the ileum in about 2 per cent of subjects. Its average position is about 1 meter above the ileocolic valve, and its average length about 5 centimeters. Its caliber is generally similar to that of the ileum, and its blind extremity may be free or may be connected with the abdominal wall or with some other portion of the intestine by a fibrous band. It represents the remains of the proximal part of the vitelline duct, the duct of communication between the yolk-sac and the primitive digestive tube in early fetal life."

Ray Shannon in the *Archives of Pediatrics*, December, 1928, says, "According to Fitz, in the newborn, it lies about 12 inches above the ileocæcal valve, while in the adult, this is increased to about 3 feet. The diverticulum may be long or short, may or may not have a separate mesentery, or may be contained within the mesentery of the small bowel. It may be fixed at its distal extremity to the umbilicus, or to any structure within the abdominal cavity. It is often conical in shape with the base large, even approaching in size the diameter of the small bowel at this point. According to Christopher, it usually has the same coats as the intestine, the mucous coat containing Lieberkuhn's gland and Peyer's patches. This same writer quotes Aschoff as saying that it may contain gastric glands, ciliated epithelium, and even pancreatic anlage. A certain number of Meckel's diverticula are associated with deformity at the umbilicus and marked deformity of the navel should therefore always bring to mind this possibility."

According to Vaughan and Singer, "Elements of gastric, duodenal, and colonic character, also glandular tissue, or pancreatic, and tissue of questionable origin may be found within the walls of the diverticulum. Of these the heterotopic structures, gastric mucosa is of greatest clinical importance since such secretions here as in the stomach have the ability to digest the intestinal mucosa, and muscularis, and lead to the formation of peptic ulcer." Mucous membrane of the gastric type is found according to Koch in 12 per cent, and according to Schaetz, in 16.6 per cent of the cases of Meckel's diverticulum. As with peptic ulcers of the stomach and duodenum, those of Meckel's diverticulum are subject to hæmorrhage, and acute perforation.

*Symptoms of Meckel's diverticulum.* The fact that this condition exists in about 2 per cent of all individuals, and very commonly is found at autopsy without having produced any symptoms indicates that, unless some pathological condition develops in the diverticulum, there are not likely to be any symptoms. The symptoms will vary according to the nature of the pathology present. The diverticulum may become inflamed just as any other part of the gastro-intestinal tract may become inflamed. If so, it may become attached by adhesions to various parts of the abdomen or any other part of the intestinal tract, and therefore, may give rise to some mechanical distortion of the small or large intestines.

In children, the symptoms more often resemble an acute appendicitis, especially when perforation has taken place, even when localized as in the case by Moolton, than anything else, and if the diagnosis of appendicitis is eliminated, then the second thought must be an inflamed Meckel's diverticulum. Inflammation may take place and cause a fibrosis at the base, with partial or complete occlusion of the bowel. The tip of the diverticulum may become attached to the umbilicus or another viscus; strangulation or torsion of the adjacent small intestine can occur and produce intestinal obstruction. Intussusception can occur from the invagination of the diverticulum. An ulcer may form and give the acute symptoms of intestinal perforation.

The most frequent symptom, however, is hæmorrhage from the bowel. When this occurs in a child it must make one think first of a Meckel's diverticulum. Vaughan and Singer state: "Symptoms referable to the diverticular ulcer prior to perforation are with the exception of hæmorrhage seldom noted. The occurrence of sudden, violent pain beginning generally in the lower half of the abdomen followed almost immediately by the symptoms and signs of a diffuse peritonitis is characteristic of a perforated ulcer. When the patient is a child, the likelihood is still greater that the ulcer is located in Meckel's diverticulum. There may be an abdominal pain particularly before meals, and relieved by food, as reported by Megevaud and Dunant, or rhythmic distress located in the right lower quadrant such as occurred one and

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Fig. 1. Examination made about an hour after giving the patient the barium mixture shows the diverticulum lying approximately over the shadow of the spinal column in the median line, approximately in the region of the umbilicus, and definitely involving the ileum. Notice the smooth outline, the large size, and the pear-shape. Case 1.

Fig. 2. The diverticulum with a longer stem, and a definite peristaltic action at the middle of the diverticulum Case 1.

a half hours after meals in Kleinschmidt's case." Melena is probably the most important symptom since the children are too young to make complaint. There may at times be profuse hæmorrhage. There may be at times abdominal cramps. In one of Shannon's cases there was slight bleeding, then improvement in all symptoms, then signs of intussusception, a palpable mass, confirmed at operation, but death in 8 hours. The patient of Dimitroff and Purkiss complained at age of 28 of headache, vomiting, and general indisposition. Tuberculosis may develop in Meckel's diverticulum as Michael records the ninth case of this complication in a white male, aged 30 years. This has always been a part of a tuberculous enteritis, or tuberculosis elsewhere, and in his case, caused a constriction in the colon, which constriction in the transverse colon was recognized roentgenologically and was thought to be neoplastic. No diagnosis of Meckel's diverticulum was made.

*The roentgen diagnosis.* Preceding this report so far as I can find there is no definite record in the literature under the heading of Meckel's diverticulum diagnosed by means of the roentgen-rays, but by correspondence, I learn through my friend, Dr. James T. Case, that he has mentioned the diagnosis of this condition under the general heading of "Jejuno-ileal diverticula," in which he says: "Only rarely have we been able to make a diagnosis of Meckel's diverticulum with the X-ray study. In a number of instances we have discovered in the routine roentgen examination signs which we thought indicated conclusively the presence of a Meckel's diverticulum, but the majority of these patients presented no symptoms indicating the need of operation, and so it has happened that once only have we been able to find at operation a Meckel's diverticulum where a pre-operative roentgen examination has led us to make a correct pre-operative diagnosis." By letter he says, "The operation was done about 4 days after the ingestion of the barium and some barium was still in the diverticulum at the end of removal." The date of the diagnosis of this case has not been mentioned.

About 2 years ago, Kantor told me that he had not made any such observations, and that he knew of no one who had made such a diagnosis. I then promised to record my observations, but it has been postponed until the present time. Since then, I have corresponded with LeWald, Hirsh, Kirklin and Camp, and none of them has diagnosed a case of Meckel's diverticulum. Schintz, Baensch and Friedl, in the third edition of their comprehensive and complete book, published in 1932, in two volumes on roentgenological diagnosis, make the statement that no such diagnosis has been made. Barclay, in his recent book, 1933, does not mention the possibility of the diagnosis of a Meckel's diverticulum. In the *Roentgen Litera-*

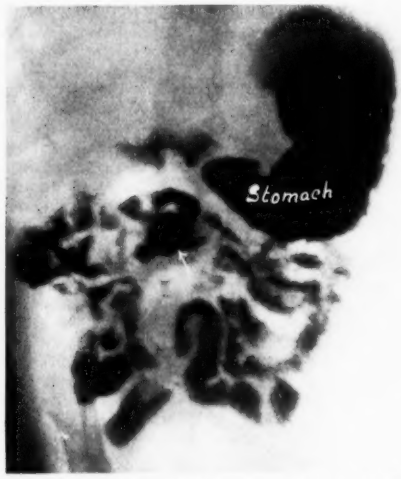


Fig. 3. A wave of peristaltic contraction at the fundus pointing downward to the left, and another wave in the neck of the diverticulum. Case 1.

Fig. 4. The diverticulum more than half empty, but still presenting smooth walls, as compared with the remainder of the bowel. Please notice that the other segments of the small intestines show progressive distribution of the barium mixture. This film has been made in the oblique position, which has thrown the diverticulum and the pyloric end of the stomach to the right of the spinal column. Case 1.

*ture*, collected and edited by Dr. Hermann Gocht, and just published January, 1934, makes no mention of the diagnosis of this condition. In the *Cumulative Index* of 1933, I find no such diagnosis having been made. Therefore, it has seemed to me advisable to record the diagnosis which I made of 2 such cases; the first 1 having been made on February 3, 1923, or approximately 11 years ago, and the second one having been made on February 2, 1931. Since presenting this material before the Philadelphia Roentgen Society on April 1, 1934, Dr. Wm. J. Corcoran demonstrated a lantern slide and referred to the case as reported by Dimitroff and Purkiss in which there was a distended loop of the ileum which led to the diagnosis and operation for Meckel's diverticulum.

Case 1. The first case was referred to me by the late Dr. Robert P. Cummins. The child was a male 7½ months of age. Three weeks before coming to my office, the patient had had two hæmorrhages from the rectum within 15 minutes. The patient was placed in the Germantown Hospital for study, during a period of 1 week. During this time the patient was seen by Drs. Charles A. Fife and Charles F. Mitchell, who could find no explanation of the hæmorrhage from the bowel. X-ray study was made but nothing abnormal was detected. However, because of the fact that the parents had lost a child 1 year of age, who died of a perforating Meckel's diverticulum 1½ years previously on the operating table, Dr. Cummins brought the patient to my office for study. I gave the patient a mixture of barium, and then watched the small intestines especially. I kept the patient in my office the whole day, and then for an additional half day, and made repeated examinations so as to catch the movement of the contents of the small bowel in every segment. On the first day, about a half hour after a barium meal, and with the child in the prone position, I found in a series of films made by instantaneous exposure, a pear-shaped body approximately 4 centimeters in length, with the base directed downward and to the right, and the stem upward and inward. This I believed to be a diverticulum. It was only shown when the patient was lying on the abdomen. I concluded, therefore, that the base of the pear-shaped body or diverticulum was located anteriorly so that when lying prone, gravity carried the contents of the intestines into this diverticulum, and when the patient was lying on the back or sides, it emptied itself and could not be shown. This diverticulum showed evidence of peristaltic contractions and, as is shown in the illustrations, the shape changed continuously. These exposures were made instantaneously, and therefore, the lines are quite sharp, but there was a continuous movement. Of special interest also, this diverticulum seemed to hold a fixed position while all the other parts of the small intestines showed the usual shifting movements.

I repeated the examination on the second day in order to get confirmation, but on the second day, I was unable to make this demonstration, probably because the diverticulum may have been filled with some other non-opaque material. I recommended operation, which was performed by Dr. Mitchell in the presence of Drs. Fife and Cummins. The following report which has been furnished to me by the surgeon, Dr. Charles F. Mitchell, is transcribed from the records of the Germantown Hospital, and will give the details concerning the operation:

The patient was brought to me because of hæmorrhage from bowel.

On February 2, 1923, the child was given a dose of castor oil because of green stools and on the morning of February 3 at 5 o'clock began to cry as if in severe pain. When the mother reached its bed, there was found a large stool, appearing to be mainly blood. About 10 o'clock that morning

Fig. 5. The stomach is filled, and the bulbous duodenum well filled. Small quantities of the barium mixture are scattered through the small intestines, and the diverticulum is recognized on the left side of the abdomen. Please notice again the smooth outline, and sac-like formation. It is unquestionably involving the small intestines, and it seems that it could be nothing else but a diverticulum. Please notice that the ascending and transverse colon as well as the remainder of the small intestines are filled with gas. Case 2.

another sanguineous stool appeared but not so much as in the previous one. The child had had no previous illnesses.

One brother died at 1 year of age during an exploratory laparotomy, following a second hæmorrhage from the bowel, the hæmorrhages being 1 month apart. Operation disclosed a ruptured Meckel's diverticulum.

Physical examination revealed a well nourished, really oversized, white, male child. The skin and conjunctivæ were normal. No glandular enlargements or deformities were present. The heart and lungs were negative. No tenderness was elicited anywhere over the body. The abdomen was naturally distended. Child was not nauseated. Treatment consisted in rest in bed, no food, plenty of water.

February 4, 1923, X-ray examination showed no evidence of foreign body in abdomen. Examination was made by fluoroscope and X-ray. February 7, 1923, the stools still showed some small amount of blood. The child was allowed to have whey and barley water. Condition was good. February 8, 1923, X-ray examination of "stomach was negative. Barium did not reveal any abnormality of small intestine. The barium in ascending colon showed some spasticity. The barium passed very quickly through the small intestine as indicated by the fact that the small intestine was not outlined. I am unable to determine the cause for hæmorrhage." H. N. Thissell.

On February 10, 1923, child left the hospital in good condition.

On March 2, 1923, patient was again admitted to the hospital—after a diagnosis of diverticulum had been made. At time of present admission occult blood was present in stools. There was no history of any considerable hæmorrhage since previous admission. Remainder of history and physical examination are as in previous history.

On March 3, examination of blood showed hæmoglobin 73 per cent; red blood cells, 2,520,000; white blood cells, 7,400; neutrophiles, 27 per cent; lymphocytes, 56; large myelocytes, 8; transitionals, 9; coagulation time, 2½ minutes.

On the same day an exploratory operation and diverticulectomy was done by Dr. Mitchell, ether anæsthesia being used. An incision was made through the right rectus muscle. The appendix while showing no signs of acute inflammation was much larger than ordinarily found in very young children. There were no adhesions, the appendix being free. *Eighteen inches from the ileocæcal valve on the upper and anterior surface of the ileum was found a diverticulum, the base of which was ½ inch in diameter, of funnel shape, about 1¼ inches long, the distal end attached to mesentery.* It showed no indications of either acute or chronic inflammation. The diverticulum was ligated across its base, resected, and the stump covered with peritoneum. No exploration, except as stated above, was made of abdominal viscera. The incision was closed without drainage.

On March 11, examination for occult blood was positive.

On March 13, patient was discharged after recovery from operation in record time without complications. However blood was still present in stools.

*Pathological report.* The specimen consisted of a small piece of intestine showing usual rugæ. The specimen had been opened so I was unable to note any constrictions. The appendix was 65 millimeters long, had been opened, showed some slight external congestion, and had a thickened mucous membrane. Microscopic examination of the appendix showed numerous large lymph nodes. The mucosa was normal in thickness, showed low grade polymorphonuclear infiltration. The outer coats were normal. Diagnosis acute catarrhal appendicitis (mild).

Section from lower bowel shows engorging of blood vessels and slight thickening of mucous coat, otherwise normal.

This child has had no symptoms since leaving the hospital and has grown up to be a fine healthy boy, now 11 years of age. It is of special interest that an X-ray examination made by a competent radiologist at the first admission to the hospital showed no evidence of any lesion of the small intestine. When examined by me 3 weeks later, the diverticulum was clearly shown in the films. Because of the struggling child no satisfaction was obtained fluoroscopically, and because of the history of hæmorrhages, we tried not to use any force. I then repeated the examination on the following day but the diverticulum did not fill with the barium. This shows that an unusual amount of work and repetition may be necessary when a diverticulum is suspected.

Case 2. A male child, aged 7 years, was brought to my office by Dr. Michael Margolies, February 2, 1931, at the advice of Dr. John B. Deaver, the family physician being Dr. John B. Farrell. The boy had been complaining of pain in the umbilical region for 3 weeks, but these pains had not been severe until 3 days before coming for X-ray examination. He had vomited on each of the two preceding days. This vomiting occurred about 5 hours after taking food. He had been having one bowel movement daily. The stools were well formed. The pains were cramp-like in character,

t between the attacks of cramps, he was feeling well. He d no fever, or chills. He had tenderness about the umbili- l region and lower abdomen, but this tenderness was not nstant. The cramps occurred 2 to 3 hours apart, but had en so severe that they awakened him at night. There was blood in the stools, and diet seemed to have no influence the symptoms. Dr. Margolies suspected appendicitis. roentgenogram of the general abdomen showed both kid- ys present, normal in size, outline, and position, and no idence of stone in the kidneys, ureters, or bladder.

The liver was normal in size, outline, and position. The leen was normal. The stomach was normal. The duode- um was normal.

Because of my suspicion that his pains were connected ith his small intestines, I studied him frequently during a eriod of 6 hours, and I found a pocket of retained barium cated 1 inch above the crest of the ileum in the left side of e abdomen which was pear-shaped, and had the appear- nces of a diverticulum. It *showed very active peristaltic ovements, but at no time during my fluoroscopic observa- ons was I able to see this sac empty itself.* This did not pply to any other part of the small intestines, for else- here I was able to see the contents move normally. A ense of resistance and fullness was found just above the rest of the ilium. A diagnosis of Meckel's diverticulum was made. A barium enema showed nothing abnormal in the sigmoid flexure, or any part of the colon, and the colon emptied satisfactorily, but this retention in the sac which I diagnosed as a Meckel's diverticulum remained even after the bowel was empty.

*The appendix itself was not visualized, but the cæcum was freely movable, and there was no localized tenderness about the cæcum.* I assumed that either the appendix was obliter- ated, or that it was so active that it did not retain the barium sufficient to be demonstrable. *In my opinion, there was no evidence of any appendicitis.* He was returned to the late Dr. John B. Deaver's care, at the Lankenau Hospital for operation, but all pains and all symptoms disappeared after he reached the hospital. He was not operated upon, and he has had no operation to the present day, and no re- currence of the symptoms. At the hospital it was found that he had a moderate grade of secondary anæmia, but normal leucocyte count, no abdominal distention, no rigid- ity, and no tenderness.

This case resembles in every way the previous one, but evidently the symptoms have quieted down, and operation has not become necessary. The diagnosis of Meckel's diverticulum certainly should be a possibility in most instances if the condition is suspected, and if sufficient, thorough and skillful work is done, keeping in mind the anatomical conditions and the varying location and the varying pathology connected with Meckel's diverticulum. We must realize that a child or adult would have to be examined in every possible position to detect a Meckel's diverticu- lum for the base of the sac may be posteriorly, anteriorly, vertically, upward or downward, or at any other angle. It may be filled with non-opaque material which would prevent the entrance of the barium and therefore remain invisible. There- fore, unless the patient's small intestines are stud- ied with this thought in mind, and in every pos- sible angle, and probably by repeated examina-

Fig. 6. The stomach is empty and the ascending and first half of the transverse colon are filled with barium. The remainder of the barium is distributed through the terminal coils of the small intestines. The diverticulum still per- sists and retains its firm, smooth outline, as distinguished from the varying walls of the other small intestines. Case 2.

tions, such a diagnosis will not be made. It is a well known fact that the studies of the small in- testines in general have been neglected. This effort to show Meckel's diverticulum may be the means of learning much else about the small in- testines that has been overlooked. Some very ex- cellent work has been done by the late Dr. Walter Mills, Dr. James T. Case and also by Dr. Lewis Gregory Cole and others, but in the great general mass of gastro-intestinal work, it has received less attention than any other part of the gastro- intestinal tract. The roentgenological charac- teristics of Meckel's diverticulum will of course be variable, but in general, they will have the characteristics that belong to any diverticulum. The diverticulum cannot be filled with a barium mixture if it is already filled with some other ma- terial. It is apt to show definite peristalsis. It is smooth in outline and it retains its position at a fixed point. The fact that a Meckel's diverticu- lum has been definitely diagnosed 10 years ago by means of the roentgen rays and again 3 years ago would indicate that it can be done again.

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# END-RESULT STUDY OF HUMERAL SHAFT FRACTURES

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IN 1925, the fracture service of the Massachusetts General Hospital adopted the system of determining and recording end-results of treated cases which is now in force. Briefly, the system consists of examining and roentgenographing each patient long enough after injury to warrant the assumption that no further changes will occur. The shortest period of observation is 1 year, while some cases, notably those involving epiphyseal injuries, are followed for many years before the end-result is decided. Each case in which the final end-result is to be noted is discussed by several members of the fracture service, and an impartial rating is agreed upon for each of three components. These are *anatomical* (based on clinical and X-ray appearance), *functional* (based on strength, presence or absence of pain, and limitation of motion), and *economic* (based on comparative earning capacity before and after injury). Each of these three aspects of the end-result is graded either 1, 2, 3, or 4 according to the 25 per cent group into which it falls, from zero per cent to 100 per cent of theoretical perfection.

The present study is based on the fractures of the humeral shaft treated between 1925 and 1931 and now properly graded as to end-result. By shaft is meant only that portion of the humerus between the surgical neck and the flare of the condyles; thus fractures through the surgical neck and supracondylar fractures are excluded. Pathological fractures will also be considered outside the scope of the present study.

There were 82 fractures of the shaft of the humerus in the 7 year period investigated, and these constituted 40 per cent of all fractures of the humerus treated. The age distribution of these 82 patients was not distinctive. The ratio of males to females was about 2 to 1. The ratio of right to left humerus was about 4 to 3. The general distribution as to type and location of fracture is shown in Table I.

TABLE I.—TYPE AND LOCATION OF 82 FRACTURES OF THE HUMERAL SHAFT

| Site | Per cent |
|---|---|
| Upper third of shaft | 29 |
| Middle third of shaft | 43 |
| Lower third of shaft | 28 |
| **Type** | |
| Transverse fracture line predominating | 50 |
| Oblique fracture line predominating | 50 |

Of the 82 cases already mentioned, only 41 are graded as to end-result and hence available for critical review. It must not be thought that these have been selected for the quality of their results, as such a selection would have defeated the purpose of the study, which is to evaluate the routine methods of treatment now in use. Due to the necessary omission of 18 patients treated in the emergency ward and consequently not graded as to end-result, cases presumably of the simplest type, and also due to the presence of cases of patients unsuccessfully treated elsewhere and sent to us months after injury, the results here reported are probably not good enough to be representative of an entirely unselected group.

## TREATMENT

The 41 cases in this series fall conveniently into 5 groups according to the method by which reduction and union were actually accomplished. It is understood that the treatment of no 2 cases can be exactly alike, so that these divisions are

TABLE II.—THREE UNREDUCED CASES

| Case | Age | Type of fracture | Site | Apparatus | End-results |
|---|---|---|---|---|---|
| 1 | 81 | Simple comminuted | Upper ⅓ | Axillary pad and swathe | Died—pneumonia |
| 2 | 60 | Simple comminuted | Upper ⅓ | Sling | $A_3F_3E_4$ |
| 3 | 7 | Simple spiral | Middle and lower ⅓ | Moulded plaster posterior splint | $A_3F_4E_4$ |

TABLE III.—EIGHT CASES REDUCED BY MANIPULATION

| Case | Age | Type of fracture | Site | Apparatus and time | End-results |
|---|---|---|---|---|---|
| 4 | 80 | Compound transverse | Middle ⅓ | Débridement; coaptation and sling to 7 wks. | $A_1F_1E_4$ |
| 5 | 9 | Simple spiral (old) | Middle ⅓ | Plaster; after-care elsewhere | $A_2F_3E_4$ |
| 6 | 30 | Simple oblique | Middle and lower ⅓ | Coaptation and swathe; then plaster to 8 wks. | $A_3F_3E_4$ |
| 7 | 4 | Simple oblique | Upper ⅓ | Plaster to 4 wks. | $A_1F_1E_1$ |
| 8 | 6 | Simple transverse | Upper ⅓ | Sling and swathe to 6 wks. | $A_1F_1E_4$ |
| 9 | 73 | Simple comminuted | Upper and middle ⅓ | Plaster to 5 wks. | $A_1F_1E_4$ |
| 10 | 65 | Simple spiral | Lower ⅓ | Molded plaster; time unknown | $A_1F_1E_4$ |
| 11 | 23 | Simple transverse | Lower ⅓ | Treated elsewhere. Entered M. G. H. for radial nerve paralysis | $A_2F_3E_4$ |

intended only to indicate related groups and are not to be taken literally.

1. *Fixation only.* It will be seen from Table II that in Case 1 death occurred before an end-result could be obtained. It is nevertheless included as a reminder that the patient's general condition may be more important than any attempt at reduction of his fracture. In this instance the patient died in spite of the very good judgment shown in doing nothing to the fracture beyond immobilizing it. One other fatal case will be mentioned later on, in which the opposite policy led to disaster. Case 2, a diabetic, also was considered too ill for reduction and was consequently left alone. She recovered, and although the position in which the fragments united was not perfect, she was able to do her housework as well as before.

It has been our experience that these extensively comminuted fractures of the upper third in old people result surprisingly well when treated only by the simplest methods of immobilization, provided care is taken to prevent stiffening of elbow and shoulder joints. Many of them are already impacted in fair alignment, and failure to unite is almost unknown.

Case 3, a little boy, presented a very different problem. This was a long spiral fracture with very little apparent displacement. No reduction or traction seemed necessary. Yet he failed to get a perfect anatomical result through the development of a varus deformity with loss of carrying angle at the elbow. One is tempted to speculate as to whether this would have happened if the arm had been treated by traction during the 2 weeks that he was in the hospital.

2. *Manipulative reduction and external fixation.* In the next group of cases reduction and union were accomplished by manipulation and external fixation alone, as shown in Table III.

Of course, this method was used in many more than 8 cases, but Table III does not include those in which manipulation was a complete failure so that some other method had to be resorted to, nor the cases in which fluoroscopic manipulation was used only as an adjunct to constant traction or operative reduction. In addition, most of the 18 cases treated in the emergency ward and consequently omitted here, were simply manipulated and put up in external fixation. Thus this group of 8 cases does not at all represent the true importance of this time honored method of treatment.

Only one of the 3 relatively poor results shown in Table III calls for any particular comment. In Case 6, the patient, a house-painter, was unruly and unco-operative because of a concomitant head injury which for several days made his fracture of secondary importance. All of the closed methods attempted during this time failed to maintain satisfactory reduction. One month after injury he was discharged in a plaster spica, which was worn for another month. Sixteen months after injury there was firm union but with considerable deformity and limitation of elbow motion. In this case the result would probably have been better if an open reduction had been done as soon as the symptoms of concussion subsided.

TABLE IV.—FIVE CASES REDUCED BY AMBULATORY TRACTION

| Case | Age | Type of fracture | Site | Apparatus and time | End-results |
|---|---|---|---|---|---|
| 12 | 32 | Simple oblique | Middle ⅓ | Jones 4 wks. then plaster | $A_4F_4E_4$ |
| 13 | 40 | Simple spiral | Middle ⅓ | Jones 1 day then plaster | $A_4F_4E_4$ |
| 14 | 13 | Simple spiral | Middle and lower ⅓ | Modified Jones 6 wks. then sling | $A_4F_4E_4$ |
| 15 | 14 | Simple oblique | Upper and middle ⅓ | Jones less than 3 wks. then sling | $A_4F_4E_4$ |
| 16 | 82 | Simple oblique comminuted | Upper and middle ⅓ | Jones 1 day then coaptation and sling | $A_4F_4E_4$ |

In Case 11, patient was treated elsewhere, only entering the hospital 2 months after injury for symptoms of radial nerve paralysis. In Case 5 patient was an epileptic idiotic child who was brought in 10 days after injury, put up in plaster, and immediately returned to the state school, where after-treatment was carried out.

It is our feeling that this method is at its best in transverse fractures in which end-to-end apposition gives a stable reduction which will not slip during the application of plaster or other external fixation. It is certainly not suited to all types of shaft fractures.

Inherent in the use of primary plaster fixation is the tendency to overlong immobilization of joints, resulting in prolonged disability for the patient. In those types of fracture where non-union rarely has to be considered, this constitutes a strong objection to the method. In those types where non-union is very common, however, namely the transverse fractures of the middle and lower thirds of the shaft, solid union in good position is the first consideration, and the long fixation and consequent difficulty of restoring joint motion must be accepted as a necessary part of treatment. It is for this reason that immediate open reduction of such fractures finds favor with many surgeons.

3. *Ambulatory traction.* Most of the oblique fractures in our series required constant traction to secure and maintain reduction. Though constant traction is always more effective with the patient in bed, there were certain cases in which ambulatory traction proved effective enough for all practical purposes. These cases are listed in Table IV.

In Table IV it will be seen that the Jones ambulatory splint was used in each case, with skin traction exerted by means of rubber tubing. In 2 cases the position secured by one day's traction was so good that a more convenient apparatus could safely be substituted. In the 3 other cases the Jones splint was worn until union occurred. All 5 had good end-results.

The desirability of some form of ambulatory treatment for the 82 year old man requires no comment. The 2 children would undoubtedly have done well with almost any method of treatment. The 2 adults, however, are instructive because of the great difference in the length of their disability. In reviewing these 2 cases it seems apparent that the prolonged disability in Case 1 was due to the prolonged immobilization, and that much time was saved by the alert management in Case 13.

Case 12. Male, age 32, oblique, middle third.
Ambulatory traction 28 days, plaster to 9 weeks.
Solid union and poor function; 12 physiotherapy treatments.
Disability 8 months.
End-result $A_4F_4E_4$.

Case 13. Male, age 40 spiral, middle third.
Ambulatory traction day, plaster to 2 weeks; then internal angular splint, coaptation splint and sling up to 7 weeks. Solid union and good function.
Disability 7 weeks.
End-result $A_4F_4E_4$.

It is worth noting that with one exception (Case 40) ambulatory traction was never attempted in a transverse fracture. We feel that constant traction is so dangerous in transverse fractures of the mid-shaft, because of non-union, that if used at all it must be carefully controlled with the patient in bed, and that the ambulatory method with its comparatively crude traction is entirely unsuited to cases of this type.

4. *Bed traction.* The largest number of patients in the present series, as shown in Table V, were treated by constant traction in bed.

All but 5 of the cases in this group were essentially oblique fractures, in which the danger of overriding was much greater than the danger of non-union. Having said so much about the danger of constant traction in transverse fractures of the mid-shaft, it seems necessary to offer some comment on the five transverse fractures in this group, all but one of which united.

Case 17 was in the upper third and was compound. The reduction accomplished by fluoroscopic manipulation was unstable. Internal fixation was not considered wise, since the wound was 24 hours old when first seen. The reduction could be maintained with 3 pounds' traction, and there

TABLE V.—REDUCED BY BED TRACTION, 15 CASES

| Case | Age | Fracture | Site | Time in bed traction | End-results |
|---|---|---|---|---|---|
| 17 | 11 | Compound transverse | Upper ⅓ | About 3 wks. | $A_4F_4E_4$ |
| 18 | 44 | Simple oblique comminuted | Middle and lower ⅓ | 4 wks. then plaster | $A_4F_4E_4$ |
| 19 | 54 | Simple oblique comminuted | Upper ⅓ | 6 wks. then plaster | $A_3F_3E_4$ |
| 20 | 37 | Simple oblique | Middle ⅓ | 3 wks. then ambulatory traction | $A_3F_4E_4$ |
| 21 | 40 | Simple transverse comminuted | Middle ⅓ | 2½ wks. then ambulatory traction then plaster | $A_4F_4E_4$ |
| 22 | 15 | Simple oblique | Middle and lower ⅓ | 2 wks. then coaptation and sling | $A_4F_4E_4$ |
| 23 | 4½ | Simple transverse | Middle ⅓ | 6 wks. then sling and swathe | $A_4F_4E_4$ |
| 24 | 26 | Compound transverse | Middle ⅓ | Débridement and Kirschner wire | Died sepsis |
| 25 | 22 | Simple oblique comminuted | Lower ⅓ | 1 wk. ambulatory traction. 2 wks. molded plaster | $A_4F_4E_4$ |
| 26 | 6 | Simple transverse | Upper ⅓ | 2 wks. then plaster | $A_4F_4E_4$ |
| 27 | 11 | Simple spiral | Upper and middle ⅓ | 2 wks. then coaptation and sling | $A_4F_4E_4$ |
| 28 | 64 | Simple comminuted | Upper ⅓ | 3 wks. then coaptation and sling | $A_4F_4E_4$ |
| 29 | 70 | Simple comminuted | Upper ⅓ | 1 wk. then plaster | $A_4F_4E_4$ |
| 30 | 11 | Simple oblique | Middle ⅓ | 1 wk. then axillary triangle and sling | $A_4F_4E_4$ |
| 31 | 6 | Simple spiral | Lower ⅓ | 1 wk. then internal angular and sling | $A_4F_4E_4$ |

was the further advantage that the wound could be readily exposed and dressed.

In Case 21 fracture could not be held reduced without traction. After 2½ weeks in bed traction, followed by a few days of very unsatisfactory ambulatory traction, patient was put into a plaster jacket. Two and one-half months after injury there was no evidence of union. Plaster cast was worn up to 3½ months, when union was solid but function was poor. The patient returned to work as a tailor 6 months after injury and still lacked 10 degrees of elbow extension 14 months after injury. Open reduction in the first place would probably have been better.

In Case 23 patient was a 4½ year old child with an unstable reduction. Non-union was considered unlikely at this age, so operation was not done, and union was solid 6 weeks after injury.

Case 26, a 6 year old child, presented a similar situation. There was perfect position and good callus after 2 weeks in gentle traction. This was protected by plaster up to 3 weeks when the patient was discharged with only a sling.

In Case 24 patient died, but it is included for the same reason that Case 1 was included. He was a sailor whose arm was caught in a power-windlass at sea, and on admission 24 hours after injury, the arm was described as a bag of bones. Unfortunately, every effort was concentrated on saving the arm. To secure alignment and at the same time allow for frequent Dakin's dressings, the arm was suspended by a Kirschner wire through the lower radius and ulna. Six days after injury multiple incisions were made in an attempt to drain a fulminating sepsis. X-rays at this time showed excellent position of the fracture. Three days later the patient died of staphylococcus septicæmia. In this case it is obvious that the fracture was treated at the expense of the patient's life. Amputation should have been done.

Skeletal traction is practically never necessary in humeral shaft fractures, since 5 to 10 pounds usually suffices, and this amount of traction can always be applied through adhesive plaster attached to the skin. Although traction transmitted through the elbow joint is in general undesirable, it was several times employed in preference to skeletal traction or open operation in cases of oblique fracture low in the shaft. Under these circumstances, traction was kept up only long enough to make slipping unlikely (1 or 2 weeks), when some form of external fixation was substituted with the elbow at a right angle.

The devices most often used for bed traction were the Thomas arm splint and Blake's suspension, usually with the arm in abduction, elbow at a right angle, and forearm suspended vertically. The average time in bed was 2.7 weeks. During this time the position of the fragments was checked by portable X-ray pictures, and if necessary, corrected by manipulation. Motion of the shoulder and elbow joints within the limits of pain was usually encouraged from the start, with the idea of shortening the functional disability.

There were 2 comparatively poor end-results which deserve a word of comment. In Case 19 the fracture was complicated by radial nerve paralysis necessitating operation 5 weeks after

TABLE VI.—FIVE OPEN REDUCTIONS DONE BECAUSE OF FAILURE OF CLOSED METHODS

| Case | Age | Fracture | Site | Original treatment | No. of operative reductions | Months of disability | End-result |
|---|---|---|---|---|---|---|---|
| 32 | 28 | Oblique comminuted | Lower ⅓ | Bed traction and fluoroscopic manipulation | 1 | 5 | $A_3F_2E_4$ |
| 33 | 28 | Transverse | Middle ⅓ | Bed traction and manipulation | 1 | 7 | $A_4F_4E_4$ |
| 34 | 23 | Oblique comminuted | Lower ⅓ | Ambulatory traction | 1 | 3 | $A_4F_4E_4$ |
| 35 | 16 | Transverse | Lower ⅓ | Fluoroscopic manipulation | 1 | About 3 | $A_4F_4E_4$ |
| 36 | 48 | Transverse comminuted | Middle ⅓ | Bed traction | 1 | 4 | $A_4F_4E_4$ |

injury and interfering with the normal recovery of function. In Case 20 a concurrent head injury complicated the treatment of the fracture enough to prevent a perfect anatomical result. Neither of these partial failures can be attributed to the method of treatment employed.

It is our feeling that this type of treatment is at its best in oblique fractures where the contact of large surfaces of broken bone makes non-union unlikely, where strong muscle pulls would, if not counteracted, produce overriding, and where no contra-indication exists for putting the patient to bed.

5. *Open reduction.* The 10 cases which came to open reduction are shown in Tables VI and VII. They could equally well have been listed as failures under the various methods of closed reduction, but it has seemed more convenient to group them together, since the discussion of some of them involves also the discussion of non-union.

In the cases in Table VI operation was not done for non-union, however, but for failure of satisfactory reduction by closed methods. Muscle interposed between the bone ends proved to be the obstacle to reduction in Case 32. At operation, 2 weeks after injury, 2 Parham bands were applied. Daily elbow exercises were started 5 days later, removing the anterior shell for the purpose. In spite of the Parham bands and the posterior plaster shell, the fragments slipped badly, so that the exercises had to be discontinued. There was then a tendency to delayed union, necessitating a long period of immobilization. Union was present 10 weeks after injury, but the full range of motion never was regained. It is hardly fair to criticize the management of this case in the light of developments which could not, perhaps, have been foreseen, but in seeking to account for the comparatively poor result, we are forced to conclude that unnecessary delay in operation and inadequate fixation were probably the important factors.

In Case 33 it was at once apparent that bed traction was unsuccessful, and a bone plating operation was done 3 days after injury. Although the eventual result was good, convalescence was prolonged by the development of an incomplete radial nerve paralysis.

In Case 34 fracture was reduced by open operation 7 days after injury and fixation was secured by a Parham band and plaster spica. The plaster was worn for 5 weeks and the patient returned to work as a chauffeur 3 months after injury, with an excellent result.

In Case 35 patient was admitted 11 days after injury with beginning union in very bad position. Instead of operating at once, an attempt was made to improve the position by manipulation under the fluoroscope and external fixation. The improved position was not maintained, however, and a bone plating operation had to be done 40 days after injury. The end-result was excellent, but the question may fairly be raised as to whether the loss of so much time before operation was warranted.

In Case 36 a severe head injury complicated recovery, so that treatment of the fracture was of secondary importance at first. Bed traction was tried and would probably have succeeded, but the patient proved too unruly to co-operate, so 36 days after injury a bone plating operation was done. Operation was still further delayed by the presence of an axillary abscess. The eventual result was excellent.

Opinions differ widely as to the place of open reduction as a primary method of choice in fractures of the humeral shaft. When carried out under the most favorable conditions, the method undoubtedly has many advantages. Our own feeling, however, in view of the uniformly good results of closed reduction, is that primary operation is seldom necessary. Perhaps the most striking fact brought out by a review of the end-results in the present series is that every patient, whatever his anatomical rating, was able to return to his former occupation. This makes us feel that the essential usefulness of the upper extremity is not entirely dependent on the presence of an anatomically perfect humeral shaft, and that the anatomical results obtained by closed methods of

TABLE VII.—TWELVE OPERATIONS DONE FOR NON-UNION IN 5 CASES

| Case | Age | Fracture | Site | Original treatment | No. of operative reductions | Months of disability | End-result |
|---|---|---|---|---|---|---|---|
| 37 | 30 | Transverse | Middle ⅓ | Elsewhere | 1 | About 18 | $A_4F_4E_4$ |
| 38 | 31 | Compound comminuted | Lower ⅓ | Elsewhere | 2 | About 26 | $A_3F_3E_4$ |
| 39 | 32 | Transverse comminuted | Middle ⅓ | Elsewhere | 2 | 32 | $A_4F_4E_4$ |
| 40 | 32 | Transverse | Middle ⅓ | Ambulatory traction | 3 | 21 | $A_4F_4E_4$ |
| 41 | 29 | Compound comminuted | Lower ⅓ | 2 operations elsewhere, 1 for non-union | 3 | 40 | $A_4F_3E_4$ |

treatment are so good that such methods should usually be tried before resorting to open operation.

COMPLICATIONS

1. *Non-union and delayed union.* The 5 cases in Table VII represent frank non-union and in several respects are the most important cases in the present series. Before discussing them in detail, it is worth noting that they had certain points in common. It is significant, for example, that the patients were all young, healthy adults, in whom the processes of repair could not have been retarded by old age or disease. It would, therefore, seem that age was definitely not a factor in the occurrence of non-union. Secondly, all of the fractures were in the middle or lower third of the shaft, recognized as perhaps the commonest site of non-union in the body. Furthermore, 3 of the fractures were transverse, and reference to the X-rays shows that in the 2 others the significant characteristic of a transverse fracture (from the point of view of repair) was also present; that is, the lack of contact between broad surfaces of broken bone.

Case 37. Patient entered the hospital 9 months after injury with an ununited transverse fracture. At operation an inlay graft was used, with an osteoperiosteal graft wrapped around the site of fracture. This attempt was successful, and solid union promptly took place. The reason for the long delay before operation is not known.

In Case 38, patient also entered with an ununited fracture 9 months after injury and was operated on, but in this instance a simple bone graft only was done. The postoperative position being unsatisfactory, another operative reduction was done 3 weeks later. Position was still unsatisfactory, but rather than subject the patient to a third operation, it was corrected as well as possible by fluoroscopic manipulation, and plaster was worn for 4 months. When the plaster was removed, union was solid, but function was naturally very poor. In spite of 99 physiotherapy treatments, function never entirely came back, and 2⅓ years after injury the end-result was $A_3F_3E_4$. A more radical operation, preferably at a much earlier date, might have obviated the delayed union with its consequent long immobilization and permanent impairment of joint motion.

Case 39 differs from the others in that non-union followed the operation instead of preceding it. The patient entered 2½ months after injury, with solid union in very bad position. The position was corrected by osteotomy and held by a 4 screw Sherman bone plate. Union failed to take place, and 6 months later a bone graft was done elsewhere for non-union. Whether or not this particular failure should have been anticipated is a matter of opinion, but it is a fact that in our experience, bone plating often is not enough to produce union in transverse fractures of the mid-humeral shaft, once the original reaction of repair has been allowed to subside.

Case 40 is the one in which patient was treated entirely on our own fracture service. Ambulatory traction was applied the day of injury, and with the additional aid of fluoroscopic manipulation 3 days later, a perfect reduction was obtained. This was put up in an axillary triangle, but 2 weeks later X-ray pictures showed that the fragments had slipped. Ambulatory traction was again applied and patient was discharged, still in traction, 4 weeks after injury. As might perhaps have been expected, no union took place. Three operations were required to secure union, the best and last being a massive bone graft 14 months after injury. The 2 unsuccessful attempts were first, end-stepping plus osteoperiosteal graft plus Parham band, and second, osteoperiosteal graft plus solid inlay graft. Solid union resulted from this operation, but later there was refracture, probably from absorption of the graft, and another operation became necessary. The end-result was good, but with a loss of 21 months. It is probable that any one of these operations would have succeeded, had it been done at the time the first reduction was lost, while the fracture was still comparatively fresh.

In Case 41 there was ample cause for non-union before coming under our care 14 months after

TABLE VIII.—FOUR CASES OF RADIAL NERVE INJURY

| Case | Fracture | Site | Onset after injury | Onset after operation | Treatment | Recovery |
|---|---|---|---|---|---|---|
| 11 | Transverse | Lower ⅓ | 4 wks. | | Cock-up and physiotherapy | Complete |
| 28 | Oblique comminuted | Upper ⅓ | | 1 day | Nerve transplanted | Almost complete |
| 33 | Compound transverse comminuted | Lower ⅓ | | Elsewhere | Elsewhere | Complete |
| 39 | Transverse | Middle ⅓ | | 4 days | Nerve explored | Practically complete |

injury. Originally a comminuted compound fracture, it had been treated by immediate débridement and removal of the loose fragments of bone. Three months later a bone graft had been done for non-union, but it had become septic and sloughed out. Consequently, on admission there was a gap of 1½ inches between rounded, eburnated, bone ends. Again 3 operations were required to secure union. The first was refreshing the bone ends and wrapping an osteoperiosteal graft around the fracture line. After 3 months in plaster there was no union. The second operation consisted of inlay plus osteoperiosteal graft, and this also failed to produce union. Five months later a massive onlay graft, held in place by 4 steel screws, resulted in union. Following this operation the patient was given cod liver oil, milk, orange juice, calcium lactate, and daily quartz-lamp treatment. She resumed work as a bookkeeper 3 years and 1 month after injury with a permanent impairment of elbow function. Had the last operation been done in the first place, there is every reason to suppose that nothing further would have been needed.

It is perhaps unnecessary to labor the point which these cases demonstrate so clearly; namely, that ordinary measures cannot be expected to meet the requirements of an extraordinary situation. Non-union is common in transverse fractures of the mid-shaft; it is favored by sepsis, by lack of proper immobilization, and by anything which prevents close, continuous contact between the bone ends. When primary union fails to occur under the stimulus of the original reaction of repair, then a situation exists which may be considered extraordinary, and which demands drastic treatment both of the local lesion and of the patient as a whole.

Delayed union, that is, union which though it occurs spontaneously, requires longer than the average time, is of course impossible to distinguish from non-union until union begins to take place or until there is evidence that it never will take place. This may require from 3 to 6 months. In the present series of 41 cases there were 4 patients not operated upon who may be considered to have shown delayed union. In 3 of them (Cases 19, 20, and 21) spontaneous union occurred at 2½, 3, and 3½ months, respectively. In Case 36 there was no evidence of union 5 weeks after injury, and as the fracture was a transverse one in the middle third, it was felt that spontaneous union was extremely unlikely to occur, and operation was accordingly done.

Taking the 5 cases in Table VII to be the only ones in which non-union occurred, as they certainly were in the 41 cases with graded end-results and probably were in the larger group of 82 treated patients, the incidence of non-union in this series may be considered to have been about 6 per cent. The incidence of delayed union cannot fairly be computed because of the lack of any generally accepted standard of normality. We feel that non-union is the most serious danger in the treatment of fractures of the humeral shaft, that it is always an indication for operation, and that the most satisfactory operation probably is a massive onlay graft fixed by screws.

2. *Radial nerve injury.* Radial nerve injury, the only other common complication, was encountered in 4 of our cases, with essentially complete recovery in all of them. This is an incidence of about 5 per cent in 82 fractures of the humeral shaft.

In Case 11 beginning paralysis was evident about 4 weeks after injury, and recovered without operation.

In Case 28 signs of paralysis appeared the day after operation, increasing for 5 weeks, when operation was done. Although the nerve was found intact, it was transplanted and recovery was almost complete, only a little weakness of wrist extension remaining 1 year after injury.

In Case 33 wrist-drop developed following débridement and removal of bone fragments elsewhere. What treatment was given is not known, but on admission 14 months after injury, no evidence of paralysis remained.

In Case 39 a bone plating operation was done 3 days after injury, and was followed 4 days later by radial nerve paralysis. The symptoms increased for 7 weeks, when operation was done. A

little scarring of the nerve was found, but no evidence of serious injury. Recovery was complete. We have seen transitory paralysis follow similar open reductions in which particular care was taken to isolate the radial nerve and keep it in sight throughout the operation. Apparently the slight stretching caused by retracting the nerve is often enough to produce symptoms of paralysis.

These cases, though the outcome was fortunate, do not illustrate the present policy of the fracture service with regard to radial nerve injury. It is agreed that immediate nerve symptoms suggest direct injury to the nerve, and that symptoms coming on several weeks after injury suggest progressive involvement of the nerve by callus. We feel that delayed progressive paralysis usually demands exploration and transplantation of the nerve. On the other hand, mild symptoms immediately following injury practically never demand operation, since they are due merely to a bruising or stretching of the nerve, and tend to recover spontaneously. If, however, there is a progressive increase in the severity of the nerve symptoms, exploration should usually be done. With regard to immediate complete paralysis there is room for a reasonable difference of opinion. If this finding can be interpreted as due to an actual severance of the radial nerve, then immediate operation and anastomosis is desirable. If, however, it implies only a severe bruise or stretch, as is almost always the case, it would probably be wiser to wait 6 to 8 weeks for beginning signs of recovery.

In general it may be said that radial nerve injury though common, is a relatively benign complication, since spontaneous recovery is the rule rather than the exception. It is highly desirable to recognize the rare case of traumatic nerve severance and repair it early. As long as any symptoms of radial nerve injury are present, a cock-up splint should be worn and the extensor muscles kept in condition by physiotherapy.

The possibility of late radial nerve involvement should be thought of, particularly in extensively comminuted fractures with wide displacement, as this consideration might occasionally influence the type of treatment. It seems reasonable to suppose that this complication would be less likely to appear, the more accurate the reposition of the fragments.

## SUMMARY OF END-RESULTS

Finally, leaving out of account all other considerations and taking the cases in this series just as they come, complicated and uncomplicated, easy and difficult, well managed and not so well managed, we see in Table IX a recapitulation of the end-results; and, after all, the end-result is the most important single criterion we have. No case was rated lower than 2 anatomically, 3 functionally, or 4 economically. Compared with other regions of the body such results are remarkably good, so that even those which are referred to here as relatively unsatisfactory might not be considered unsatisfactory at all when compared with the results of fractures in general.

TABLE IX.—SUMMARY OF END-RESULTS IN 41 CASES

| Cases | | |
|---|---|---|
| $A_4F_4E_4$ | 28 | 80 per cent satisfactory |
| $A_3F_4E_4$ | 3 | |
| $A_4F_3E_4$ | 1 | |
| $A_3F_3E_4$ | 5 | 20 per cent *relatively* unsatisfactory |
| $A_2F_3E_4$ | 2 | |
| Died | 2 | |

It is quite surprising to find that these end-results were influenced so little by age; in fact, the results in the older age-group were actually better than those in the younger. Similarly, non-union in this series was seen only among young adults, often persisting in spite of repeated operations; while in marked contrast was Case 4, an 80 year old woman who got spontaneous union of a compound transverse fracture of the mid-shaft, with the bone ends projecting and the brachial artery and median nerve exposed, after being discharged against advice on her twenty-eighth day with her arm in only coaptation splints and a sling!

The only other significant generality that emerges from an analysis of the end-results is concerned with the type of treatment. The group treated as bed patients had better end-results than those treated as ambulatory patients, in spite of the fact that the former group contained most of the difficult cases.

## CONCLUSIONS

1. When intelligently treated by any suitable method, the end-results of fractures of the humeral shaft are excellent.

2. In general, transverse fractures should be reduced by manipulation (closed or open) and held by fixation (external or internal); oblique fractures should be reduced and held by constant traction; and comminuted fractures should be treated by the simplest method suited to the individual case.

3. Constant traction is dangerous in transverse or short oblique fractures, especially where they occur in the middle and lower thirds, and should be used only with great caution, if at all, under these circumstances.

4. Bed traction is always more effective than ambulatory traction, but is not always necessary. Ambulatory traction may be well applied by means of the Jones humerus splint, and bed traction by means of the Thomas arm splint or Blake's suspension.

5. Primary open reduction as a treatment of choice, though sometimes desirable, is not often necessary. The indications for early operative reduction are: (a) failure to accomplish or maintain satisfactory reduction by closed methods, and (b) anticipated non-union.

6. Bone plating alone will not bring about secondary union after the original reaction of repair has subsided, as it will in a fresh fracture. Bone grafting is usually necessary.

7. Persistent delayed and non-union is the greatest obstacle to the successful operative treatment of old ununited fractures. The patient should be given the maximum chance for union at the time the first operation is performed, by the use of a radical procedure combined with the vigorous employment of the various common systemic aids.

8. Non-union may reasonably be anticipated when, in a transverse or short oblique fracture in the middle or lower third of the humeral shaft, there has been no contact between the bone ends during the early period of active reaction of repair (usually about two weeks).

9. Radial nerve injury rarely results in permanent disability.

# EDITORIALS


## SURGERY, GYNECOLOGY AND OBSTETRICS

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DECEMBER, 1934


## MODERN ANÆSTHESIA

SURGEONS have been so accustomed to look upon anæsthesia as but a minor part of the operative procedure that they must be watchful lest they fail to realize and to make use of the part modern anæsthesia is playing in recent surgical developments. Surgery during the last two decades has made extraordinary strides, and, while it is still making gratifying progress, its early rate of progress has of necessity slowed down somewhat.

Anæsthesia and anæsthetists, starting from the time when there was no anæsthesia (not such a great number of years ago) and from the time when ether was the sole anæsthetic (but a few years ago), are at the present time in a state of rapid, practical, and very gratifying advancement.

Having had an interest in anæsthesia for several years, and a close association with physicians whose entire time has been devoted to anæsthesia and its relation to surgery, the part anæsthesia and anæsthetists have played, and are playing, in improving surgery and surgical results, has been impressed upon me. I have also had the opportunity to realize and appreciate that through the field of anæsthesia and anæsthetists there still remains throughout this country and abroad an opportunity to improve surgical procedures greatly from the point of view of the patient's comfort and safety, the ease and facility with which the operation can be performed, and the end-results as they relate to mortality as well as morbidity.

Lest this editorial be construed as an argument against the nurse anæsthetist, I wish to state that in my opinion, nurse anæsthetists under experienced physician anæsthetists' supervision are not only desirable but necessary. Well trained nurse anæsthetists under the supervision of physician anæsthetists can and do give most satisfactory and safe inhalation anæsthesia and serve to maintain anæsthesia costs at lower levels, a point of no small importance to the patient, the hospital, the surgeon, and the progress of anæsthesia.

We have but to view the available types of anæsthesia and to mention some of their special advantages to realize how important this field is in a surgical procedure. We would not consider operating upon a patient with intrathoracic goiter without intratracheal anæsthesia, knowing as we do that delivery of a large thyroid tumor from the chest often produces tracheal obstruction, that if tracheotomy is necessary after the mediastinum has been opened, a mediastinitis easily results, and that with intratracheal anæsthesia such an emergency cannot arise.

The department of chest surgery in this clinic definitely attributes its low mortality rate, particularly in thoracoplasty for tubercu-

losis, at least in part to the fact that these patients are anæsthetized with the hydrocarbon anæsthetic cyclopropane, to the fact that cyclopropane, anæsthetic mixture, has an oxygen percentage of 90 in contradistinction to the nitrous oxide anæsthetic mixture with an oxygen percentage of 9, and to ethylene anæsthetic mixture with an oxygen percentage of but 15, and to the fact that even though these patients must lie on the one good lung, it is possible with this anæsthesia with its rich oxygen content to maintain the patients in this position with pink color and to keep them well oxygenated.

Avertin, permitting as it does the arrangement of the apparatus after the patient's return to his bed, has been a real boon to the orthopedic surgeon as well as to the general surgeon.

We in general surgery feel very strongly that the employment of intratracheal ethylene anæsthesia, combined with regional infiltration of the abdominal wall with metycain, has made subtotal and total gastrectomy safer and so more possible than when ether or spinal anæsthesia were employed.

No longer do we hear, nor should there ever be heard, any statement as: "I use spinal anæsthesia entirely." Spinal anæsthesia, in experienced hands, has a real place even in abdominal surgery, particularly in acute appendicitis and intestinal obstruction. In upper abdominal surgery it also has a place, particularly for the good risk patient and in the operation which will not take over an hour. It is not a desirable form of anæsthesia for poor risk patients or for those needing long operations because of the surgeon's inclination to demand high levels of anæsthesia and a length of anæsthesia demanding large doses of the drug. Surgeons are sometimes unconscious of the disadvantages of these events. They are so delighted by the relaxation, the quietness, and the ease of exposure with spinal anæsthesia, that they sometimes unwisely employ high and long spinal anæsthesia, a method associated with serious drops in blood pressure and dangerous states of shock.

A variety of special types of anæsthesia, of special advantage, can be mentioned as advantageous in surgical procedures, particularly the employment of sacral anæsthesia in electrocoagulation of the prostate and operative cystoscopy, cervical block in the operation for œsophageal diverticulum and the savings of gas in goiter operations with the carbon dioxide extraction apparatus. For example, it is stated by our anæsthetists that to do a goiter operation without the carbon dioxide extraction apparatus requires, on the average, 85 gallons of ethylene and oxygen while with this apparatus but 15 gallons are required, a saving of 70 gallons of gas per operation together with a distinctly better anæsthesia. In the anæsthesia of patients having goiter operations alone in our clinic, this arrangement saves us seventy thousand gallons of ethylene per year and gives a better anæsthesia.

Individual surgeons, and hospitals with surgical services, who wish to keep in step with the progress of surgery must appreciate that it is advantageous to encourage a limited number of men in a community to interest themselves in and become expert with the various number of methods of anæsthesia. Likewise, surgeons must be willing to cooperate with these men in their development as anæsthetists and in the employment and selection of new anæsthetics in cases in which they would be helpful.

Good anæsthesia costs more than poor or mediocre anæsthesia, but a surgeon or a hospital acquiring the advantages of the modern developments in anæsthesia will very soon appreciate that they have been more

than repaid for the investment in terms of the patients' satisfaction, mortality, morbidity, and the surgeons' and hospitals' comfort of conscience. FRANK H. LAHEY.

## PREPAYMENT PLAN FOR MEDICAL AND HOSPITAL SERVICE

PREPAYMENT plan for medical care for those falling in the moderate income group is one of the problems calling for most careful study by the entire profession and all its organizations. Canada and the United States are both confronted with the question. Help is being urgently demanded by the people, and by civic and philanthropic organizations. The question is rapidly assuming national importance in both countries and unless the profession approaches the problem in a prompt and constructive manner, poorly judged plans will be forced upon the practitioners of medicine. We should all have an open mind until some solution has been arrived at that is satisfactory to both the profession and the public.

Dr. Greenough, in his presidential address at the recent meeting of the American College of Surgeons in Boston, turned his attention to this vexing problem. The full text of his remarks will appear in a later issue of the Journal. Meanwhile, we may quote his well balanced conclusions.

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No single health insurance plan of national scope appears at present to be applicable to the conditions existing in this country. The matter is at present one for local study and experiment; in which the best medical and surgical ability in the community is needed, acting in co-operation with others qualified by their knowledge of economic conditions to join in the study of the problem.

Individuals of the lower level income classes in the moderate means group, for whom some support derived from the community to supplement any possible prepayment insurance plan may possibly be needed, are the ones for whom the provision of efficient medical and surgical service offers at this time the greatest difficulties. With further progress in health education those in the upper level of the moderate means class may well develop an interest and a desire to participate in voluntary prepayment plans, beginning first with hospitalization alone, and extending ultimately perhaps to full medical, dental, and nursing services.

It is greatly to be desired that the trial of these new methods of providing medical and surgical service to the community should be encouraged in different communities where the co-operation of the hospitals, the medical profession, and others interested in the maintenance of the public health can be secured. Certain general principles which should be observed in the organization and operation of these plans have already been approved by the College. The hospital department of the College provides a ready means of securing accurate information in regard to these plans and their operation which should continue to be utilized to accumulate facts on which future judgment may be based.

While the advantages and disadvantages of the different plans for health insurance are under investigation in this laboratory of experience, a number of other steps are immediately open to us which should be of material help in providing more efficient service.

1. The value of the code of ethics of the medical profession in the protection of the interests of the whole population must be more widely appreciated by the public.

2. The medical and surgical care of the indigent sick must be recognized everywhere as an obligation of the community.

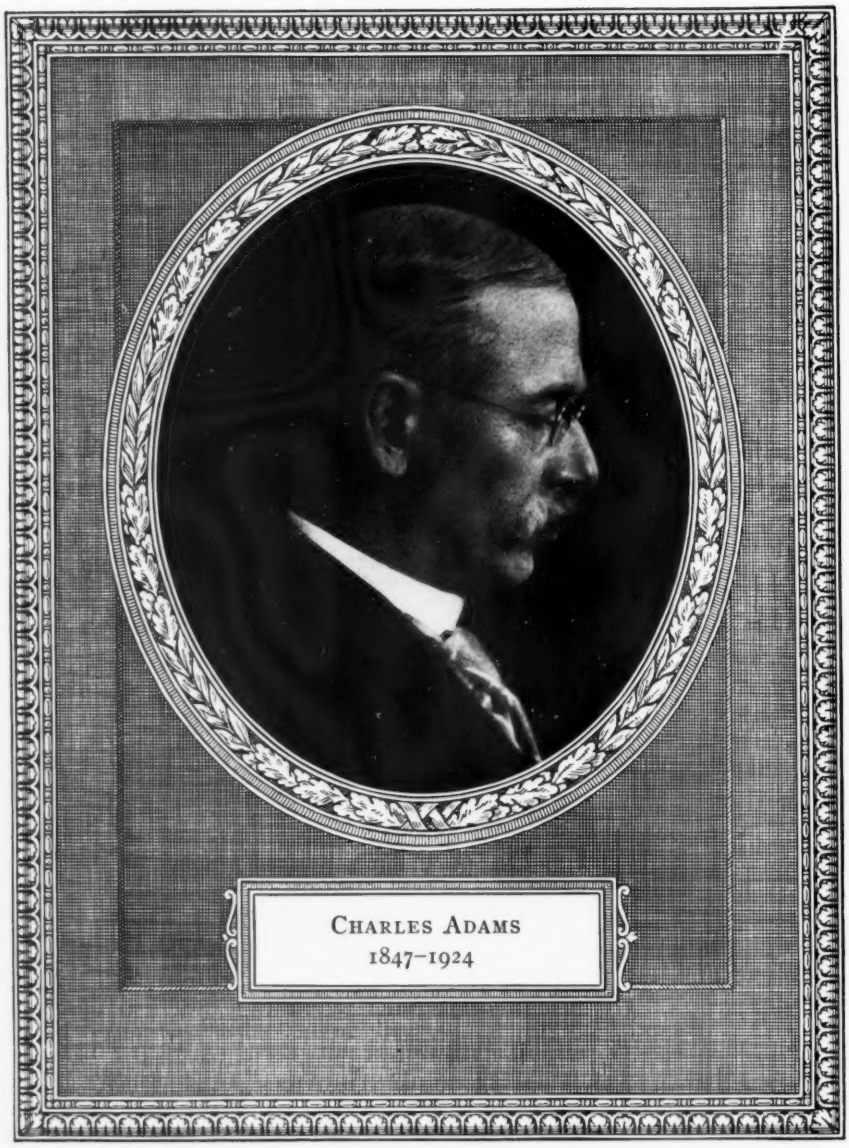
3. The segregation of hospital wards for patients of moderate means, who can and should pay minimum hospital expenses and reduced fees, should be more widely practiced.

4. Abuses of hospital charity by those who can afford to pay must be prevented.

5. The expansion of the activities of public health departments into the clinical field should be restricted to demonstration clinics for educational purposes; and to such other activities as can be made available to the community only by the use of public funds.

6. The education of the public in regard to health matters and the postgraduate instruction of physicians should be more widely developed, and finally

7. The quality of service supplied to the community should be recognized both by the public and by the medical profession as the first and most important consideration in every plan which is formulated for providing more efficient surgical service and for making this service available to all classes of the population.



CHARLES ADAMS
1847–1924

UNIV. OF MICH.

# MASTER SURGEONS OF AMERICA

## CHARLES ADAMS

IN the summer of 1924, a group of doctors gathered at a dinner in the Army and Navy Club of Chicago, with the object of formulating a memorial to their friend and teacher, Charles Adams, the source of much inspiration, to them especially as regards the finer things in the practice of surgery. After some discussion it was found that each of those assembled had been touched in a personal and intimate manner by his contact with Dr. Adams and so it was decided that each should write a letter telling what he felt Charles Adams had done for him in shaping his career. The opinions varied greatly and showed in how many ways Dr. Adams with his great fund of knowledge and experience had helped his students. This incident does much to show the character of the subject of this sketch.

Charles Adams was born in the village of Flore, Northamptonshire, England, May 29, 1847, the county that gave to America the families of George Washington, Benjamin Franklin, William Penn, and Henry Wadsworth Longfellow.

Charles had three brothers and one sister. His father, John Adams, was a rugged English farmer and stockman. His mother had been a teacher in a private school and was a woman of superior education. It is interesting to note that the father furnished the physical stamina, industry, and keen knowledge of men, while the mother brought culture and desire for study.

When Charles was 9 years old, his family came to America and settled in Milwaukee and from there moved to Chicago, where the father continued to deal in cattle and later helped to found the stockyards. At the age of 17 years, young Charles began work in his father's office, but he continued his studies. He also found work under Dr. Stimson at the Chicago Academy of Science whenever he was free from his duties at his father's office. I believe that it was here that he gained the impetus that later made him a fellow of the Royal Microscopical Society of England, and in his medical career a careful student of pathology. It is a well known fact that the microscope became a close companion in his declining years at Honolulu.

Dr. Adams graduated from Hahnemann Medical College, Chicago, in 1872, he served a year in the hospital, and then set out for the medical centers of London, Glasgow, Edinburgh, and Paris—goals of young surgeons of ambition of his

day. A young scientist is fortunate if he falls under the spell of great leaders in his profession, and Dr. Adams was particularly fortunate in this respect. In later years he told his students many anecdotes regarding the great teachers of Europe.

Dr. Adams returned to Chicago to take up general practice and at this time he married Mary, the daughter of Thomas S. Curtis, of Wellingborough, England. They had one son, Cuthburt, and a daughter, Ethel. Mrs. Adams died in 1888. In 1889 Dr. Adams married Mrs. Elizabeth Gaylord, widow of Henry Gaylord and daughter of W. H. Mitchell. From 1874 to 1875 he was professor of surgical pathology in Hahnemann Medical College; from 1875 to 1884, professor of the principles and practices of surgery in Chicago Homeopathic Medical College. In 1896 he gave up general practice and devoted himself exclusively to surgery.

Dr. Adams was one of Chicago's pioneers in the study of pathology. Even in the eighties he maintained his own laboratory and later employed from one to two technicians to run through for his microscope every tissue that came from his operating table.

In 1898 he received the degree of M.D. (*ad eundem gradum*) from Rush Medical College. He was consulting surgeon to the Chicago Nursing and Half Orphan Asylum, the Evanston hospital, Streeter Hospital, St. Joseph's Hospital, and for over 25 years surgeon to the Cook County Hospital.

He was a member and past president of the American Association of Military Surgeons, fellow of the Royal Microscopical Society of England, fellow of the American College of Surgeons, the Chicago Surgical Society, the American Medical Association, the Illinois Medical Society, and the Chicago Medical Society.

He was an omnivorous reader and accumulated a large library both of medical and general. In addition to the standard editions he was always on the lookout for rare and ancient medical books. He had a reading acquaintance with six languages and read the journals in each. In the early days of Chicago, transportation was slow and much time was lost in going about from hospital to hospital. Adams always carried a canvas leather bound bag that held a few of his latest medical magazines and read as he rode or waited for a bridge at the river. Until I came under the influence of Osler I thought him the best read medical man in general literature I had known. To have him join the family circle and read to us from the classics or some modern writer was a treat.

Adams succeeded Nicholas Senn as surgeon general of Illinois. An unusual friendship had sprung up between these men which probably was little known among their associates. Both had brilliant minds and common interests—general and military surgery. They served together in the Spanish War. Both had been presidents of the Association of Military Surgeons. Senn had a dramatic personality and an enormous capacity for work. Adams was quiet and unobtrusive. Each carried on experiments in surgery and there was a constant exchange of

opinions and experience between them. Senn's notable contribution was bone healing. Adams carried on a series of experiments both before and after the Spanish War on gunshot wounds of the abdomen. In his home for many years on a high bluff on the shores of lake Michigan, north of Chicago, he carried out these investigations. With all the military rifles that he could obtain he worked out the results of bullets of different trajectory, velocity and density, using dogs as experimental material, striking their abdomens at all possible angles.

Watching him in the operating room, one was amazed at his dexterity, but this came from constant practice in and out of the hospital in tying knots and in the manipulation of clamps and instruments. In the nineties a general surgeon was expected to do a cataract operation and a laparotomy on the same day and highly trained hands were necessary to be successful.

Adams edited Senn's *Principles of Surgery*, wrote notable papers on gunshot wounds and general surgery, and reviewed the surgical literature of his day. His avocation was the collection of cartoons and rare books. Of the two, the former seemed the most absorbing. Through agents he gathered cartoons from every country where cartoons were published. His collection he carefully classified over a period of years and presented to one of Chicago's public libraries.

When War was declared he was past 70 but he offered his services and was accepted.

His declining years were spent in Honolulu in his beautiful Japanese home overlooking the sea. Here with his books and microscope he classified the flies on the island and studied the deep sea crustacea.

An analysis of Charles Adams' character shows an abhorence of ostentation, a dislike of publicity, but deep friendship for those near him, and an idealism which characterized his whole professional life. WILLIAM MCI. THOMPSON.

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

IN the book[1] by Dr. Crile recently published he develops the theme that certain diseases of civilized man are due to excessive activity of the brain-thyroid-adrenal-sympathetic system, which he refers to as "the kinetic system" of the body. The author maintains that modern "high speed living" overstimulates the "kinetic system" until it tends to dominate destructively the entire body. It is suggested that man, through orthogenesis, may in time be destroyed by the same organs which have enabled him to gain such great control over his external environment. This thesis is developed by pointing out and emphasizing certain selected features of the comparative anatomy, embryology, and physiology of the brain, adrenals, and thyroid. The diseases referred to particularly are neurocirculatory asthenia, hyperthyroidism, peptic ulcer, and diabetes, a chapter being devoted to each. The author would treat these diseases by "rationalization" and rest, but when these fail, he would break the "vicious circle" in the "kinetic system" by denervating the adrenals. The operative technique for adrenal denervation is given in detail. The precautions to be taken are enumerated and the complications emphasized. Two hundred and thirty-three pages are devoted to the case histories of 307 patients in whom the adrenal glands were subjected to operation alone or in combination with thyroidectomy or sympathectomy. The operation has been done for epilepsy, hypertension, and psychoneurosis as well as in the aforementioned diseases. The author makes the claim that adrenal denervation is of some value in all these conditions except psychoneurosis, in which it is contra-indicated. As the author states, this "dekineticizing operation" introduces a new principle, or at least a new surgical procedure, into medical thought and practice. The case reports with accompanying charts and illustrations constitute the sum total of evidence in support of the author's contention that adrenal denervation has been used successfully "in the treatment of recurrent hyperthyroidism and of certain cases of primary hyperthyroidism, in the treatment of persistent or recurrent peptic ulcer, and in the treatment of a limited series of cases of diabetes," and as a "routine method of treatment of neurocirculatory asthenia." A critical reader will very probably obtain the impression that the author has not proved his case because of the equivocal nature of much of the evidence advanced. However, the reader's interest will be sustained, even during the perusal of the case histories, by the charming style of the presentation and the provocative nature of the theory and evidence submitted.

Certain chapters in the book have been contributed in part or in whole by Drs. E. S. A. King, George Crile, Jr., E. Perry McCullogh, James Hudson Dunlap, and N. F. Hicken. A. C. Ivy.

[1] DISEASES PECULIAR TO CIVILIZED MAN; CLINICAL MANAGEMENT AND SURGICAL TREATMENT. By George Crile, M.D. New York: The MacMillan Co., 1934.

AS stated in the preface, the book[2] by Vehrs constitutes a survey of the experimental and clinical records in the field of spinal anæsthesia for the past 49 years. The author sets forth in as simple a style as is possible to describe the complicated nervous system, its various reactions and responses to spinal anæsthesia. He emphasizes the importance of having a thorough understanding of the nerve control of the heart, vessels, and respiratory system. Throughout the book he emphasizes the value of allowing the blood to gravitate to the heart by keeping the patient in the Trendelenburg position during the operation.

Methods to assist the heart and respiration and their vital centers during spinal nerve block are considered. The various methods of producing analgesia and anæsthesia are briefly discussed and a method of the author is described in detail. Sensory nerve block is separated from motor nerve block and considered as an entity under the title of regional spinal analgesia. An excellent comparison is presented as to the relative merits of spinal and general anæsthesia that all advocates of the latter would do well to review. At no time in spinal anæsthesia under similar conditions are the patient's body cells subjected to the degree of acidosis and poisoning by blood urea, nitrogen and blood sugar which occurs in ether anæsthesia. Ether merely causes unconsciousness with little or no prevention of shock.

The indications and contra-indications for spinal anæsthesia are clearly presented as well as a tabulation of its advantages. The illustrations are good and numerous charts and diagrams are presented to clarify the text.

The reviewer feels that, with the tremendous interest that has been aroused in this subject within recent years, this compact volume will be well received. He believes that too many surgeons have condemned

[2] SPINAL ANESTHESIA; TECHNIC AND CLINICAL APPLICATION. By George R. Vehrs, M.D. St. Louis: C. V. Mosby, 1934.

spinal anæsthesia after a brief trial because of failures due to a lack of proper understanding not only of the anatomy and physiology and of the various laws involved, but also because of an improper technique. Frequently the method has not been at fault but rather its application. Spinal anæsthesia when properly used is undoubtedly our safest and most ideal anæsthetic and will doubtless remain such until superseded by the progress of science.

The reviewer appreciates that several excellent methods are being used in administering spinal anæsthesia and that the essential factor is to master one of them. The method described by the author is undoubtedly a good one but would not appear as satisfactory as the one familiar to the reviewer. The all important injection of ephedrin in the interspinous muscles 5 minutes preceding the spinal tap, the use of carbon dioxide to control nausea, the importance of an accurate ratio between the dosages of ephedrin, novocain, and the amount of spinal fluid in governing the height and duration of spinal anæsthesia are but briefly considered. The necessity of the early and continuous use of the Trendelenburg position during the course of the operation and following it is not essential to the method used by the reviewer.

These points, however, are concerned merely with a difference of technique and to gain a real knowledge of the science of spinal anæsthesia anyone interested in the subject can greatly clarify his knowledge of the question by a review of this volume.

ARNOLD JACKSON.

THE study of chronic sinus infection as related to systemic disease is portrayed[1] in a very readable, and thorough manner by Watson-Williams who has had a vast clinical experience and has made accurate observations.

Special emphasis is placed upon the value of suction—exploration whereby a cannula is placed in the infected sinus and the contents aspirated. This has proved of great value therapeutically as well as diagnostically.

While the book is essentially designed for the specialist, the busy practitioner will also find it helpful in solving some of his problems. It is complete in every detail, and should be read by every one interested in focal sepsis. JOHN F. DELPH.

[1]CHRONIC NASAL SINUSITIS AND ITS RELATION TO GENERAL MEDICINE (Chronic Sinusitis and Systemic Sepsis). By Patrick Watson-Williams. 2d ed. Baltimore: William Wood & Co., 1933.

THE present widespread tendency of publishing books written by a group of men is followed in the book[2] by Adair and Stieglitz. Adair, as is well known, ranks among the first few authorities on obstetrics in the country, and Stieglitz for many years supervised the medical care of a large number of obstetrical patients at the Chicago Lying-In Hospital. Hence a book published by such authorities should be of exceptional merit, and this is unquestionably so. The authors enlisted the aid of 37 other individuals, 29 of whom were specialists in the various branches of medicine, and 8 of whom were obstetricians and/or gynecologists. The authors have succeeded admirably in their effort to "coordinate and correlate the medical knowledge concerning the problems of diagnosis, therapy and prognosis of diseases occurring coincidentally with pregnancy." Due to the fact that each chapter was edited by an obstetrician and also an internist, both medical and obstetrical viewpoints are presented.

The book is divided into twelve sections, each of which is devoted to a special branch of medicine. The longest chapter is that devoted to diseases of the blood, and this seems disproportionately large. The chapter on tropical diseases is excellent but with the exception of the 6 pages devoted to amœbiasis and dysentery, the remaining 28 pages are devoted to diseases which are almost unknown in this country. In the section on diseases of the heart, Herrmann advocates cæsarean section under local anæsthesia for certain cardiac cases. The reviewer is most enthusiastic about the use of local anæsthesia in obstetrics and gynecology, but he would like to point out that not infrequently in patients with bad hearts there is a sudden and dangerous rise in blood pressure when the patient is being delivered under local anæsthesia, either abdominally or vaginally. Hence, care should be exercised in the selection of cardiac patients for local anæsthesia.

These minor criticisms cannot detract from the excellence of the book which will prove most useful to all physicians who practice obstetrics and to all specialists who see pregnant women in consultation. The book, undoubtedly, will be a boon to practitioners in small communities where few specialists are available. The authors are to be highly commended for their contribution, and the publishers deserve praise for the way the book has been compiled. J. P. GREENHILL.

[2]OBSTETRIC MEDICINE; THE DIAGNOSIS AND MANAGEMENT OF THE COMMONER DISEASES IN RELATION TO PREGNANCY. Edited by Fred L. Adair, M.A., M.D., F.A.C.S., and Edward J. Stieglitz, M.S., M.D., F.A.C.P. Philadelphia: Lea & Febiger, 1934.

# AMERICAN COLLEGE OF SURGEONS

## THE IMPORTANCE AND VALUE TO SCIENTIFIC MEDICINE OF ANIMAL EXPERIMENTATION

THE American College of Surgeons is presenting herewith a series of articles by recognized authorities, articles which set forth the importance and the value of experimental research—research which deals with life itself, and which will continue to advance human health, human usefulness, and human happiness for all time to come.

In the words of that eminent citizen, Charles W. Eliot:

> "The number of animals used for the benefits of the human race in making possible the "recent advances of surgery and medicine is insignificant, indeed infinitesimal, compared with "the number used for human food and human service; but the benefits to mankind which "result from animal experimentation are immeasurable in quantity, and very precious in "quality. The benefits of the discoveries go on, generation after generation, multiplying "as they go."

Animal experimentation has conferred immense benefits upon mankind, and doctors themselves have volunteered as subjects when animals have not afforded suitable media for experimental research.

Experimental research is one of the brightest pages in medical history, and it must not cease if the welfare of humanity is to be furthered, and if medical progress is to continue.

FRANKLIN H. MARTIN, M.D., Director General.

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SIR FREDERICK G. BANTING, Department of Medical Research, Banting Institute, University of Toronto, Toronto: I may say that I believe in animal experimentation because I think human life is more valuable than animal life. Medical science cannot advance without the use of animals. The work on diabetes and insulin could not have been done without the use of dogs.

I believe that every experiment should be well thought out and thoroughly planned before it is carried out. In carrying out survival experiments on animals, the same care should be used with regard to asepsis as in the case of the human. It has always been our practice to administer an anæsthetic to an animal before any operative procedure is carried out. The postoperative care of the animal is as important as in the case of the human. The attendants who care for the animals should be naturally fond of and kind to animals. In addition, workers should be either fully qualified or thoroughly trained before being permitted to do operations on animals.

If the above principles are carried out, the pain caused to the animal is minimized and the greatest amount of information gained.

WALTER B. CANNON, George Higginson Professor of Physiology, Harvard University Medical School, Boston: The antivivisectionists hold the following beliefs: (1) that animal experimentation in laboratories of medical research is hideously cruel, (2) that either no value has come from it that justifies its continuance or if value has come it is morally wrong to profit therefrom.

The claim of cruelty has not been proved. For nearly a quarter-century rules requiring the humane treatment of experimental animals have been adopted, posted, and enforced in laboratories of medical research throughout the United States. Convinced of the real humanity of investigative methods the deans of medical schools and the directors of medical research institutes announced 10 years ago the "Open Door" policy according to which persons who had seen surgical operations would be permitted to visit the laboratories at any time and witness the proceedings. The antivivisectionists, not directly acquainted with what they write about and so ignorant of scientific description that they constantly misinterpret it, prefer to use their perverted imagination instead of learning the facts. No wonder the English

Royal Commission declared that their lurid accounts of laboratory methods were calculated to mislead the public.

The claim that no value has come from animal experimentation is contrary to the formal declarations of international and national organizations, of special medical and surgical societies, and of students and observers of medical history. Any one who will read the admirable collection of papers written by experts in various aspects of medicine and published by the American Medical Association, will find in them convincing evidence of the immense value of animal experimentation in the diagnosis and treatment of disease, and of the consequent incalculable benefits to both lower animals and human beings. Any statement to the contrary is stupidly and absurdly false.

The claim that animal experimentation, even though beneficial, is morally wrong, is in opposition to the ethics of our civilization. We kill calves and take their mothers' milk; we slaughter annually hundreds of thousands of cattle, sheep, and hogs; we castrate male creatures without anæsthesia, merely to make them more tractable or to please our palates; we hunt and trap with every possibility of inflicting pain. In the face of these habits, there is no reason why the use of animals in laboratories, with care to avoid causing unnecessary discomfort and with the object of increasing knowledge and lessening human misery, should be regarded as specially immoral. Indeed the fact that animal experimentation has vastly reduced the suffering of mankind and that, if persisted in, it will continue to do so, renders the work of medical investigation highly moral—even a moral duty.

ANTON J. CARLSON, Chairman, and Professor of Physiology, University of Chicago, Chicago: Informed laymen are well aware that animals are built on the same plan as man; they have the same organs working by the same nervous and chemical machinery. They subsist on the same kind of food and the same kind of air as man and are subjected to the same kind of disorders in the living machine as man. The causes and effects of disorders of the heart, the stomach, the lungs, the eyes, the nerves, or the brain are essentially the same in animals and man. When the experimental method was introduced in science, including the science of medicine, experiments on animals resulted in rapid progress of our understanding of the nervous and chemical machinery operating in the body in health and of the disturbances of this machinery that lead to disease. Thus, animal experimentation has played a very great rôle in the development of our knowledge of infections and their control, of anæsthesias and their refinement, of disturbances in nutrition and dietary deficiencies, in the development of new drugs and their continued refinement.

There were more than 30 years of intensive research on animals before we had the substance insulin in sufficient purity to warrant its trial on diabetic patients. Every informed layman now knows the value of insulin in diabetes in man. These facts are so obvious to informed people that they would scarcely need restatement except for the additional fact that there are among us a small group of partly misinformed, partly peculiar people who oppose and would prevent all experiments on animals as cruel or useless, the so called "Antivivisectionists." This propaganda against progress in medicine sometimes goes under the name of "humane education."

Cruelty is useless infliction of pain. Every normal adult human being is opposed to the useless infliction of pain, be it to man or animals, but pain, unfortunately, is a part of life, in the case of man, both mental and physical pain, and in the case of animals, in all probability at least, physical pain. The misinformed or misguided opponents of animal experimentation in medicine and biology would have you believe that nothing of value to man has come through animal experimentation and that animal experimentation is cruel and useless. The facts are these—while we may point with pride and cheer to the progress in our understanding of life processes, the disturbances of these processes, which we call disease, and the control of disease, the fact remains that our knowledge of the causes and methods of control today are very incomplete. This is true of almost every disturbance or disease. We could probably control all diseases better if we knew everything connected with their causation and complications more completely. Some of these factors in disease appear now to be tied up with heredity and while we seem to know the A B C of heredity, largely through experiments on plants and animals, we do not know the whole alphabet. It appears to me that people who today can hold such views, that animal experimentation has been useless in the extension of our knowledge of the causes and control of diseases, are either exceedingly misinformed or exceedingly peculiar people. It appears very clear to me that we must study every page of nature's book before we throw up our hands in despair at achieving a society freer from disease, from pain, from defects that at present render life unhappy both in man and beasts. Let us not forget that animal experimentation has

made almost as much progress in working out the causes and control of animal disorders as of disorders in man.

Finally, we have the accusation that research biologists and physicians who resort to animal experimentation to further human knowledge are practicing cruelty to animals. In the first place, many of the experiments are of the so called acute type where the animal is put under complete anæsthesia during the observations and is never allowed to recover from the anæsthetic. There can be no cruelty in such a process. This includes all animals used in teaching or practice training for physicians and surgeons.

In the second place, there are chronic experiments involved in research calling for operative interference with this or that organ—these animals are put under complete anæsthesia during the operation, the operations must be aseptic as in similar operations on humans, and the animals cared for after operation as completely as human patients.

In the third place, a great many experiments on animals in the field of nutrition or in the reaction to drugs involve no cutting or opening of the body. They may involve the slight momentary discomfort of a hypodermic injection, that is, a needle prick or a mosquito sting in man.

To call such investigative methods cruelty seems to me to indicate loss of the sense of proportion. They do not call for specific prohibitive legislation in the city, state, or nation over and above our common humane laws. In practical life animals, as well as plants, must be adjusted primarily in the interest of man. We do so necessarily in the case of bacteria, flies, rats, insects, and all manner of wild and domestic animals. In my philosophy, man comes first. I will gladly contribute to shelter for stray or uncared for dogs when my fellow humans, and particularly children, are adequately cared for, but I am unable to account for the repeated charge of cruelty of animal experimentation and cruelty in the experimenter by apparently sane people who do not take the trouble to visit the university laboratories and the hospitals where such experiments are going on, or take the trouble to investigate the reputation for cruelty of the individual investigator. Some of the finest specimens of men and women that it has been my privilege to meet in my long life have been investigators in biology and medicine, particularly by methods of animal experimentation, and such well known humane citizens as Dean Gilkey and Rabbi Mann have for years upheld and defended the necessity and utility of animal experimentation in medical research and medical teaching.

ALEXIS CARREL, Member, The Rockefeller Institute for Medical Research, New York: Every civilized human being should support the American College of Surgeons in its endeavor to check the activities of the National Anti-Vivisection Society. Once more, well meaning but ignorant people have banded together to oppose the progress of science. Such an event has often occurred in the course of history but it is particularly dangerous at this time. Although we are effectively protected against plague, yellow fever, cholera, typhus, tetanus, typhoid fever, diphtheria, etc., we are still exposed to countless diseases. Almost all misery comes from illness,—illness of the mind as well as the body. Modern man is suffering from cruel, lingering diseases, such as cancer, heart lesions, diabetes, Bright's disease; feeblemindedness, insanity, and criminality. He often has not enough vitality and intelligence and is often too weak to face the difficulties of existence. We do not know as yet the precise causes of these evils. We have to discover them. But we cannot experiment on human beings. Even if experimentation were possible, its results would be too slow and it would take one hundred years to ascertain the effects on a group of human beings of a given diet, of a given chemical, or a given mode of education or of life. The experiments on guinea pigs, rats, and mice, which live a much shorter time than man, have helped a great deal. These animals, however, are very different from us; their intelligence is rudimentary. We must use monkeys and dogs for the elucidation of the human problems—the problems which concern both the body and the mind of millions of people. Biological research is our only hope of learning how to protect human beings against suffering and death. Would those who wish to deprive scientists of their weapons against disease advocate the disarmament of the entire police force of the United States, and the free play of gangsters against the public?

GEORGE CRILE, Director, Cleveland Clinic, Cleveland, Ohio: The rarity of disease in animals is to a large extent due to scientific researches planned for the purpose of discovering the cause and method of prevention of such diseases as tuberculosis, cholera, and rabies. These researches have been carried on by subjecting animals to the necessary experimentation. It is apparent, therefore, that domestic animals have profited greatly by experiments made upon themselves in scientific researches.

Among the animals that have received the greatest benefit from experimental medicine is

the dog. One of the great menaces to his life, a disease which has produced great distress in its slow torturous death, is rabies. This disease has now been practically eliminated as the result of experimentation upon the dog himself. The distemper also that affects so many dogs has been now largely cured as the result of experimentation upon dogs by means of which the cause of distemper has been discovered and a vaccine for its treatment has been developed. If the dog himself were to make a statement regarding the use of a limited number of his own kind for the discovery and the cure of a disease that menaces him, he would be just as much in favor of this practice as is the human being, just as in the case of yellow fever and of other diseases in which human beings have sacrificed themselves in an effort to discover their causes and to devise methods of prevention and treatment.

The enormous number of cases of sickness and death among the two billions of human beings always present on the earth has actually contributed to the welfare of the dog and other domestic animals for, as the result of the study of the cause of the diseases that affect human beings, the domestic animals also have benefited. The principles of surgery and preventive medicine which are applied to man are as effective when applied to dogs and cats and horses by the veterinarian. Moreover, the dog has benefited from the use of other animals in the experimental laboratory where a vastly larger number of rats, mice, guinea pigs, and rabbits are used; the number of these animals used, in proportion to the number of dogs, being certainly not less than 1,000 to 1.

Neither man himself nor any one species of animal is entitled to be excluded from taking his part in the drama of life. Certainly our guest animal, the dog, should carry a little of the burden.

D. J. Davis, Dean, University of Illinois College of Medicine, Chicago: Before the beginning of human dissection the ancients acquired much valuable information in anatomy, physiology, and surgery from studies on the lower forms of life, especially the domestic animals.

During the renaissance period, many fundamental discoveries such as the circulation of the blood by Harvey were made largely through animal experimentation and especially on dogs.

The greatest single discovery leading to the alleviation of suffering and pain, that of anæsthesia, was initiated, controlled, and perfected mainly by properly devised animal experiments.

The early career of Lord Lister, the renowned discoverer and promoter of antisepsis, was occupied with the studies of such problems as the "Early Stages of Inflammation," the "Physiology of Involuntary Muscular Fibers," the "Coagulation of the Blood," and the "Nature of Fermentation and Putrefaction"; all based more or less on animal experiments.

Every one should be familiar with the history of animal plagues which in every age has led to untold suffering and death to countless millions of animals both wild and domestic. Often these widespread epidemic diseases involved human beings. They are referred to in the *Bible* and in the annals of every people. Such diseases exist today and many are readily transferred to humans. Examples are anthrax, glanders, dog distemper, tuberculosis, hydrophobia or rabies, and undulant fever. At the present time in all civilized countries these diseases are now either under control or are being rapidly eradicated. Every honest person, even to some degree familiar with the facts, will admit that this control of the great animal and human epidemics with the accompanying alleviation of pain, suffering, and misery in both animals and man is due in the main to knowledge acquired by the study and experiments on animals by both medical men and veterinarians.

The value of serums and vaccines for the prevention and cure of disease is known and conceded by all intelligent persons. Their discovery and use marks this age as the great humanitarian era. For the control and prevention of such diseases as infantile paralysis, encephalitis (sleeping sickness), pandemic influenza, typhus fever, Rocky Mountain spotted fever, and many other recent and ancient diseases, our only hope lies in the use of vaccines and serums. Already note the advances made in the prevention of Rocky Mountain fever by a tick vaccine for which discovery recently the annual gold medal of the American Medical Association was awarded.

Loyal Davis, Professor of Surgery and Chairman, Division of Surgery, Northwestern University Medical School, Chicago: The antivivisectionist should commune with himself and answer these questions honestly. Am I willing to refuse all medical or surgical treatment for myself, or my children, the value, results, and methods of which have been learned from animal experimentation? Am I willing to subject my child to a death rate of over 50 per cent in the treatment of diphtheria which resulted before the discovery and standardization of antitoxin as compared to the present mortality rate of two deaths per million of population? Am I willing to subject my infant to the ravages of whooping cough rather

than see that child relieved by the injection of serum? If my child or I became afflicted with diabetes, am I willing to refuse the administration of insulin, discovered and perfected by animal experimentation? Is the expectant mother of today ready to suffer the pains of labor without the benefit of alleviation of that pain by methods first tested upon animals? Am I willing to forego all of the therapeutic and diagnostic advances in the treatment of lung, heart, and metabolic diseases which have been discovered by trial and error experiments upon animals? Am I willing to take medicine, unstandardized in dosage, because of lack of animal experiments?

The antivivisectionist who can answer all of these and scores of other similar questions in the affirmative, and then practices what he preaches may be lacking in wisdom but at least he is no hypocrite.

N. S. DAVIS III, Assistant Professor of Medicine, Northwestern University Medical School, Chicago: Many of the advances in medicine and surgery during the past century have been connected with animal experimentation.

The surgeon has learned much of what he is able to do by performing operations on the smaller mammals. As a result, he has acquired technical skill and a knowledge of how much can be done without endangering the animal's life. In the preparation of prophylactic and therapeutic sera for commercial use, animal experimentation is necessary. Because of the sensitiveness which many people acquire after receiving an injection of one type of animal serum, it is advisable that sera for different diseases be made from different animals. Sera of great value in the treatment of diseases of animals have also been developed as a result of experimentation. Furthermore, it is impossible to assay such drugs as digitalis and insulin except by the reaction of the experimental animal to a given amount of each preparation. Merely weighing or measuring the amount of the substance does not give this information. Insulin could never have been produced commercially and could not have come into general use in the treatment of diabetes if a method of assaying had not been developed. Digitalis has become a much more effective drug since it has been standardized by its effect on animals. The physician is now able to know the effective dose he is prescribing without much regard to the weight of the digitalis in the dose; he prescribes units of digitalis rather than grams of digitalis, just as he prescribes units of insulin rather than cubic centimeters of insulin solution. Animal experimentation has also been of great value in determining the potency of extracts of the various glands of internal secretion. This is especially true of some of the extracts of the ovary that are proving to be of great therapeutic value.

Little if any progress along any of these lines could have been made without animal experimentation. Anything that would make it impossible for such work to continue would not only stop progress in the medical sciences but would also cause a regression to conditions that existed before animal experimentation was developed.

WILLIAM H. FELDMAN, Assistant Professor of Comparative Pathology, The Mayo Foundation, Rochester, Minnesota: In the United States in 1914 hog cholera caused losses estimated at $100,000,000 and made swine husbandry a decidedly uncertain and hazardous business. By animal experimentation there was made available anti-hog cholera serum and by the use of this product the loss of hogs in the United States was reduced from nearly 12 per cent in 1914 to approximately 4 per cent during the succeeding 5 year period. At the present time, by proper procedures of immunization nearly 100 per cent protection may be secured. This is only one example in which the use of animals in experimental medicine has been of inestimable value to the livestock industry. Experimental procedures in which laboratory animals have played significant rôles have also made possible the production of agents for the protection of farm animals against such diseases as black-leg, anthrax, and tetanus. In addition, experimental methods that would have been impossible without the use of animals have netted results that provide the dog owner with means to protect his pet against canine distemper and rabies. Valuable information concerning serious and often fatal forms of internal parasitism of dogs and other animals has also been obtained by use of laboratory animals.

The sum total of the gains made in controlling and eradicating the infectious diseases of the domesticated animals by the use of experimental animals is so impressive as to leave no doubt as to the soundness of this method of research.

To prohibit the use of animals in laboratory procedures would be disastrous for the livestock industry, since it would be no longer possible to:

1. Manufacture anti-hog cholera serum and test its potency.

2. Test the potency and safety of biologic agents designed to protect cattle against blackleg.

3. Prepare products for the protection and treatment of animals and man exposed to or affected with anthrax.

4. Produce and test the potency and safety of antitetanus serum.

5. Prepare agents for immunization against rabies.

It would seem neither humane nor economically wise to relinquish the advantages science has finally achieved in the attack against diseases that have long occasioned tremendous monetary losses as well as distress and suffering to both animal and man and which finally have been brought under control by animal experimentation.

SIMON FLEXNER, The Rockefeller Institute for Medical Research, New York: We are used to being told that we are today living in a new world. We are even used to being told, just at the moment, that there is doubt whether the conditions of the new world in which we live are better, indeed they may be worse, than those of the world in which our parents and their parents lived their lives.

However that may be, socially or economically considered, I am confident there can be no doubt that our state, medically regarded, is far better today than in any previous period of the world's history. This fact I feel requires no undue emphasis. There is today less illness in relation to the population, with fewer deaths and longer expectation of life than ever before.

While all this is true and perhaps quite generally known and appreciated, it is not as generally understood as it should be, how these great changes and improvements in health have been brought about, and what greater improvements and benefits may be expected in the next period, if the science of medicine is permitted to continue its progress free from the hampering restrictions and obstructions which certain misguided persons would put in its path.

Suppose, for the sake of comparison, that we imagine ourselves back in the year 1870, which in this country was in the period immediately following the Civil War, during which vast experience was gained in medicine and surgery as understood and practiced at that time. These experiences, by no means pleasant to contemplate, are described in records and biographies of the hospital surgeons of the time. We shall be transported into a period before bacteriology became a science; before the amazing discoveries in bacteriology of the Frenchman Pasteur and the German Koch had disclosed the germ nature of wound infection and the contagious diseases; and before the Scotch surgeon Lister, basing his investigations on the discoveries of Pasteur, had introduced antiseptic, soon changed to aseptic, surgery into practice. There are still living a few surgeons who can recall the horrors of those distressing days, when wound infection was rampant, and compare them with the present state of surgical practice, so safe and widely employed that no part of the body, not even the heart and brain, are considered too sacred to be forbidden the exploration of the surgeon's knife. In those earlier days, surgery was limited almost wholly to operations on the surface and extremities of the body; to invade the interior was to invite almost certain disaster; it was to be undertaken only by the boldest and most expert surgeons, and then only when not to operate was even more hazardous than to do so.

All this was changed by the medical research of Pasteur and Lister and Koch in the next quarter of a century. Their investigations, carried out chiefly in the laboratory and at first on animals, provided the scientific foundations for present day bacteriology and operative surgery, the technique of which has gradually been perfected, extended, and taught, until every city and town has the inestimable benefit of the skilled diagnosis of disease and skilled surgery when needed.

There is no opportunity to deal with details. The knowledge of bacteriology was acquired slowly, and for its acquisition demanded the unremitting labors of very talented men, who succeeded not only through inspiration and effort, but even against much opposition. I have indicated that the discoveries in bacteriology provided the explanation of the sources of wound infection and thus led to the perfection of surgical, operative technique. These discoveries also led to the explanation of the nature of the common infectious and contagious diseases. Just as wound infection results from the presence of one class of bacteria at the site of operation, so do the infectious and contagious diseases result from the presence of particular bacteria within the body.

Those were great days in the last decades of the nineteenth century, which brought to light and opened to experimental study the bacteria producing tuberculosis, typhoid fever, diphtheria, and epidemic meningitis, to mention a few notable examples only, and led to the fundamental discoveries in immunity to disease. From the knowledge resulting from these laboratory discoveries we can date those improvements in public health administration which have had so potent an influence in reducing the number of cases and the fatalities of such common infectious diseases as those already enumerated; and, as by-products (and notwithstanding the fact that their germ

causes were revealed 20 or more years later) of measles, scarlet fever, and other contagious diseases of childhood.

There is great temptation to introduce figures into this story; but space forbids. I must, however, mention one startling change in the prevalence of a disease formerly so destructive among children. In 1894, before the use of diphtheria antitoxin was introduced, 4,530 persons in New York City died of this disease, which is at the rate of 163 per 100,000 of population. In contrast to these figures are to be placed those of the year 1932. In that year there were 212 deaths from diphtheria, or 3 per 100,000 of population.

These are triumphs indeed, the effects of which may be read on every hand in the tables of mortality among infants, children, and adolescents, and which have led to an increase of at least 12 years in the individual expectation of life in the culturally advanced countries. For a time this progress, if not arrested, was at least greatly diminished in speed. The reason was that the improvements in the public health which resulted from the amazing discoveries in bacteriology affected chiefly the infectious diseases of early life, and the extent and safety of operative surgery. The effects of these discoveries and the practical health measures based on them were experienced in individuals approximately up to the thirty-fifth to the fortieth year of life. The benefits were thus limited, because the diseases of past middle life present another character and are due chiefly to causes other than those of the diseases of earlier decades.

Just now, and after an interval in which the science of physiology had first to be further built up—precisely as the science of bacteriology had to be developed in the earlier years—progress in the control of disease has been resumed. In this intervening period, physiologists have disclosed the function, or mode of action, of a group of glands of the body, called "ductless" because of their anatomical structure, which had remained enigmas for hundreds of years. The normal action of these glands is essential to the maintenance of health, and their derangement is responsible, as we have now learned, for serious and fatal diseases as age advances. It is because of the discoveries regarding the nature of the thyroid, adrenal, and pituitary glands, and of certain secondary but similar essential activities of such organs as the pancreas and liver, that increased control is being achieved of certain diseases of past middle life, among which diabetes and pernicious anæmia may be singled out for mention. We are in the beginning stages of this advance at the present time; progress is almost continuous at the moment; a bright hope has, therefore, awakened in the hearts of informed physicians and laboratory investigators that the next years will witness a still greater acceleration of the control of chronic disease, compared with which the progress already made, considerable as it is, will appear to have been only a beginning.

Here also are triumphs, to be converted into still greater achievements, if the growth of science is to continue unimpeded. You will have perceived that I have omitted to mention still other successes of magnitude in regard to the prevention and cure of disease, which result from the discoveries relating to vitamins, light rays, and chemical products or drugs, of which much might be related.

And now, what is it that the experimenter in the laboratory does that has yielded so much already to mitigate disease, improve health, and lengthen life, and why is the continuation of his work unfettered by injurious restrictions so essential to further progress? The experimenter studies disease on the lower animals whenever possible, and always under controlled and humane conditions. He seeks to discover the nature of the conditions responsible for disease, just as the chemist and physicist seek to discover by experiment the nature of the phenomena of matter. There are only two ways of learning about things: observation and experiment. For centuries, very learned and gifted men sought to learn about disease from observation alone; the modern medical era which, in spite of its brevity, has triumphed so gloriously over all past eras, has progressed through the employment of the experimental method. By this method, the element of control is introduced into observation; thus it is possible to learn what is happening at any stage of disease, and to utilize this knowledge for the understanding and the better management of disease itself.

Great as is the progress of which I have been speaking, there are hard problems immediately ahead to which answers, at least sufficient answers, have not yet been obtained. I have pointed, with what I hope is pardonable pride, to the decrease in such diseases as tuberculosis, typhoid fever, and diphtheria; but what is to be said of cancer, Bright's disease, and diseases of the heart and blood vessels? You all know how seriously prevalent and destructive these diseases are. There is no lack of effort being made to reach a fuller understanding of their nature, origin, and control; and I believe that progress is being made. The ultimate goal seems, however, still distant; there is but one way, I submit, to bring that goal

within reasonable hope of being reached finally—and that is by continued, unremitting, unobstructed study by the experimental method.

A final word. This paper seems to deal with disease in man, and it does. But every essential thing which it covers can be applied equally to disease in animals and even in plants. Everywhere in this country are institutions, supported by state or federal funds, in which animal and plant pathology are being studied. The advances which have so far been made and which are continuing and becoming ever more rapid, have gone hand in hand with the advances made in the study of diseases of human beings. There are no closed compartments in nature into which man, animals, and plants can be separately placed. All are related organically and, as we may say, united physiologically and pathologically. A blow struck at experiments to solve disease in man is felt immediately by those who are endeavoring to prevent disease in animals and plants, and *vice versa*. Koch developed tuberculin in the hope that with it he would benefit sufferers from tuberculosis among men; today herds are freed of tuberculous cattle by injecting tuberculin into them in order to disclose hidden foci of disease. The malign operation of mosquitoes and other biting insects in conveying disease germs is the same in principle in Texas cattle fever, in malaria and yellow fever in man, and in virus diseases of plants. No essential biological division exists between man and the lower animals and plants, whether in respect to health or to disease. If, therefore, we would learn, and through learning grow more powerful and effective to prevent and to cure disease, to lengthen life, and to increase happiness through security in all its varied forms, then we should endeavor to act dispassionately and wisely in promoting the advance in knowledge which alone can free us still further from the evils of disease.

HERBERT FOX, Director, Pepper Laboratory of Clinical Medicine, Philadelphia: Having been engaged for many years in observational and investigative comparative pathology and bacteriology and as the officer in charge of a responsible clinical laboratory, I know that I understand better the problems of health and disease in man because of the careful use of lower animals in investigation for comparison and contrast. My laboratories have used all kinds of animals and I know that there has been a good reason for the investigation or it would not have been done and I know the animals have been kept in as good condition as my own home animals.

In a clinical laboratory of an important hospital, no day passes in which there is not a demand for the use of animals to solve the difficult problems that are presented. Communicable disease can often only be safely discovered by the use of animals. In order to discover if vaccines and antiserum are safe to put into human beings, they must be tried upon animals. In order to discover if the apparatus and technique of departments where surgical operations are done are entirely safe, they must be checked by the use of animals.

In solving the many obscure clinical cases that are referred to the modern hospital, it is frequently obligatory that the tests be carried out by the use of animals and these are the principal but not entire list of services that the animal can yield to the sick man for his diagnosis and treatment.

Furthermore, I know that the well man of today and of the future is not safe unless he has at his disposal the protection that comes by a knowledge of normal and abnormal processes as seen in the lower animals, which means that he would not be safe without the experimentation that can be carried on in laboratories.

EVARTS A. GRAHAM, Professor of Surgery, Washington University School of Medicine, St. Louis, Missouri: Not a single accredited doctor of medicine, or medical school or university in this country has ever raised a voice against vivisection. Is this failure to oppose the practice due to the fact that these groups are any less humane than other groups of society? No. It is due rather to the fact that those who are best qualified to understand realize fully that experiments on the living animal are essential to progress in the war against disease whether that disease affects only human beings on the one hand or animals themselves on the other. In the light of the amazing conquests achieved in that war by the use of vivisection how can anyone now cry "Stop!" and try to tie the hands of those investigators who are finding ways to prevent the pain and the mutilation of little children, that is still caused by disease! As it happens, moreover, in practically all of the work in vivisection, the animal suffers no pain because the experiment is carried out in full anæsthesia from which the animal is not allowed to recover.

Have the doctors any axe to grind in favoring vivisection? Is there any selfish reason for their failure to join the ranks of the antivivisectionists? The only results to be effected from animal experimentation are a better understanding of disease, its nature, its causes, its treatment, and even its

prevention. Can anyone call it a selfish motive for the doctors to work for the elimination of disease and thereby diminish the need of their services to the public?

Antivivisection campaigns are usually chiefly directed against the use of dogs. It is easy to understand the sentimental feeling against the use of this faithful and trusting animal for such purposes. But yet the use of dogs is often essential for the purposes of investigation. Are dogs of more value to us than our children?

STUART GRAVES, University of Alabama School of Medicine, University, Alabama: Many of our domestic animals are raised that man might live. Antivivisectionists, as well as others, eat the flesh of these animals without hue and cry.

Many of the objectors to animal experimentation have undergone some form of surgical operation that their life might be saved or prolonged. Had it not been for animal experimentation, especially upon dogs, the present degree of perfection in surgery would never have been made possible. There is no objection to an operation upon the ground that the sacrifice of an experimental animal made the operation possible. Operations upon the brain, stomach, liver, gall bladder, appendix, pancreas, spleen, kidneys, arteries, veins, nerves and spine, and the successful use of various forms of anæsthesia owe their origin as well as their success, with few exceptions, to animal experimentation.

During the Civil War the mortality rate incident to abdominal wounds was over 90 per cent. *There were no abdominal operations.* Surgical knowledge and experience was vague and meager. During the World War the mortality rate from abdominal wounds was only 43.32 per cent.

Abdominal wounds in the latter were more grave owing to the nature of projectiles used. Had it not been for knowledge and experience gained, and perfected surgical technique developed through the use of dogs as the subject of the experiment instead of man, the World War mortality rate from abdominal wounds would have exceeded that of the Civil War.

Had it not been for the use of dogs, Banting and associates would never have given insulin to the world to prolong the life and preserve the health of diabetics. It would be interesting to know the percentage of diabetics among the antivivisectionists using insulin.

Objection is often made to animal experimentation upon the ground that it is not humane. This is sheer ignorance of fact. Experimental animals, in medical schools and other investigational institutions, are well fed and cared for. Cages and runs are well cleaned and aired. Their environment is far better, for the most part, than many of our less fortunate fellow human beings, toward whom the antivivisectionists could well afford to turn in a helpful way instead of throwing a stumbling block in the progress of scientific teaching and investigation which seeks to lessen human suffering. Experimental animals are not allowed to suffer. No operations or procedure that might prove painful are done except under anæsthesia.

If animal experimentation is to be prohibited the world will go back to practices of the dark ages. We will rely upon tokens, charms, superstitions, the fighting of evil spirits, and the call of the occult in vain attempt to promote health and prolong life. Medical schools would close, health departments would cease to exist. The sick and death rate would be appalling. Can the world at large afford to suffer because of the intellectual dishonesty of a misguided few?

J. P. GREENHILL, Associate Professor of Gynecology, Loyola University School of Medicine, Chicago: During the last few decades animal experimentation has yielded an enormous amount of valuable information to the study of childbirth. Through experiments on animals and chiefly through this means, we have gathered a vast fund of knowledge concerning menstruation, the entire process of reproduction, the transmission of substances from mother to offspring and vice versa, childlessness, miscarriages, the action of X-rays and radium on the newborn child, monstrosities, twins, anæsthesia during childbirth, childbed fever, and the effect of diet on the mother and baby. While the amount of this information is very extensive it is still insignificant compared to what is still to be learned. For the solution of most of these problems, animal experimentation is absolutely essential.

SAMUEL C. HARVEY, Professor of Surgery, Yale University School of Medicine, New Haven, Connecticut: The alternative to experimentation upon animals, and in particular dogs, is a very simple one, and that is experimentation upon man himself. Progress in knowledge of disease and its treatment cannot be stopped by the passage of antivivisection legislation, for the necessity of it is too obvious both to the physician and his patients, but it can be seriously hindered. The result will be the trial on man himself of procedures that had far better be first carried out on an experimental animal. Anyone who opposes properly conducted vivisection must either in all conscience be willing

to submit himself in place of an animal for experimentation or take the stand that no further progress in medicine shall be made, for such cannot occur without the determination of the truth by the method of trial and error. It is strange indeed that individuals exist who can face with equanimity the suffering and death of their fellow-men or who do not cavil at the mutilation and killing of animals for commercial purposes, but become consumed with indignation at the thought of animal experimentation carried out by the most benevolent of professions for the good of humanity.

J. Shelton Horsley, St. Elizabeth's Hospital, Richmond, Virginia: No surgeon or physiologist desires to give unnecessary pain to any animal. Aside from the humane aspect, the performance of an experiment on an animal struggling and suffering is difficult and tends to make the result of the experiment uncertain. In every well established laboratory all major operative procedures are carried out under some form of anæsthesia. In order to do successful surgery, not only must the mechanical technique of an operation be mastered, but the surgeon should know the physiologic function of the tissues with which he is dealing in order to preserve or readjust the function.

If a child has an obstruction of the bowel, or a man a strangulated hernia, or a wound in the stomach or intestine the problem of immediate surgical relief at once arises, probably removing a portion of the intestine and sewing the ends together. No one can learn to do this solely by reading about it, or by hearing someone tell about it, or even by seeing someone else do it, any more than he can learn how to pitch a curved ball, or to serve a game of tennis, by reading about it or by seeing it done. It requires the actual experience in the performance of the operation on living tissue. No matter how carefully the work may be done on the dead tissue of a cadaver, there is nothing that substitutes for living tissue. The result of the experimental operation can be ascertained only by observing the animal after the operation.

The surgeon, then, is reduced to the choice of learning how to repair injured bowel on the lower animals, or of acquiring skill by his experience on human beings. If an experimental operation is done on an animal and the animal dies a postmortem examination is made to determine the cause of death. If the animal recovers it is killed under anæsthesia after a number of days and the site of the operation is studied. In this way the technique of the operation of suturing the intestines may be so improved that the surgeon can, with confidence, undertake this operation on a human being.

It is well known that the mortality rate in the first series of experimental operations on animals is higher than it is later on after the operator has become more skillful. If he is denied the opportunity of acquiring this skill by experimental operations on the lower animals, he must obtain it by clinical experience on human beings, and many lives will be needlessly sacrificed before the necessary training is obtained. This, of course, is only one feature of the benefits of animal experimentation, but it is very practical and striking.

Dogs eat about the same food and have somewhat the same habitat as man, and often make the best subjects for many of these experiments. The stray dogs that are gathered in a pound and killed help no one. If these animals are properly taken care of in a laboratory, operated upon painlessly, and painlessly killed, they are of great use to humanity. The cook who wrings a chicken's neck to obtain a pleasing meal, the butcher who cuts a steer's throat for a tender steak, the hunter who kills big game for amusement or traps animals for their furs, all seem to have at least the tacit approval of many of those who object to animal experimentation. Surely the world would seem topsy-turvy if it is permitted to slaughter animals for our pleasure or appetite while the careful performance of painless experimental operations to lessen disease and to decrease the suffering and death of human beings is forbidden.

Robert M. Hutchins, President, University of Chicago, Chicago: The history of biology and medicine during the last three centuries shows that experiments on animals have played a very great rôle in advancing man's understanding and control of the processes of life in health and disease. The leaders in biology and medicine inform me that the continued use of animals is necessary in the application of much of what is known to the diagnosis, control, and cure of disease in man and animals. Furthermore, a large territory of the unknown still lies ahead of the biological and medical investigators. It seems altogether reasonable that biology and medicine of today and tomorrow should have the same freedom and support as in the past. We cannot indict the biological and medical investigators (and the institutions that sponsor their labors) on the evidence of cruelty to animals and futility in results so far offered by the opponents of animal experimentation in medical teaching and research. Very large funds, public and private, are devoted to the advance of biology and medicine

by the leading universities, medical schools, and hospitals. A small group of essentially misinformed people should not be permitted to impede the service of these trusts for the benefit of mankind.

A. C. Ivy, Nathan Smith Davis Professor of Physiology and Pharmacology, Northwestern University Medical School, Chicago: Within the past 60 years remarkable, yea, almost miraculous advances have been made in our knowledge of physiology and of the cause, cure, and prevention of disease. Still, everyone knows that much is yet to be accomplished. Since most of these advances have come either directly or indirectly from the use of the scientific method of animal experimentation, and since no substitute method has even been suggested, it is obvious that the future progress of medicine depends to a large extent on the use of this method.

In regard to the legitimacy of this method, I adhere to the general belief held by medical scientists, namely, that man has the moral and ethical right to use dumb animals humanely for useful experimental purposes in order to avoid random experimentation on man, and that there are very definite limits to the experimentation that should be permitted on human subjects, whether they be patients, students, or teachers.

When the opponents of animal experimentation have sought to have laws made to abolish all animal experimentation, medical scientists have pointed out to the legislators that they must answer two questions before they vote. First, is the search for new methods of diagnosing and treating disease to continue? Second, if so, is the basic, preliminary, and often random experimentation to be done on man or animals?

After ascertaining that legislative assemblies will not prohibit animal experimentation, the opponents of animal experimentation next seek exemption for the dog. (They, thus, imply that their chief aim, as many claim, is to hamper the progress of medical science rather than to "save" the dog from experimental laboratories.) Now, in addition to their charges of cruelty in and lack of profit from animal experimentation, they can make an emotional appeal to the sentimental attachment that we all have for our dog. They fail to point out that people's pet dogs are not used, that only stray dogs without home, owner, or friend and condemned to be destroyed are used. Although all states have anti-cruelty laws, an indictment of cruelty has never been returned against a medical scientist, and, to say that nothing of profit has come from the use of dogs is to say that the lives of many people now living are of no value.

The continued use of dogs for experimental purposes is necessary for several reasons, lack of space not permitting detailed examples. First, their size renders it possible to perform operations and experiments that could not be performed on smaller animals. Second, the structure and function of most of their internal organs are identical with and react to drugs as those of man. Third, the dog is much better adapted to laboratory life than, for example, the pig. Fourth, in large cities, where medical schools and research institutes are found, dogs are wantonly but necessarily destroyed daily at the pound, while if they were humanely used in the research laboratories, their destruction would be of service to both man and animal kind.

It should be remembered that most all we know about blood pressure, the lungs, liver, stomach, intestines, gall bladder, pancreas, parathyroids and adrenals, and much that we know about the heart, kidneys, spinal cord, brain, and metabolism, have come from experiments on the dog. The discovery of insulin, which will prolong the lives of more than one million people living in the United States today, was made possible almost entirely by experiments on the dog. The discovery of the liver treatment for pernicious anæmia, formerly an insidiously fatal disease, came from experiments on dogs. The discovery of cortin, which prolongs the lives of patients with Addison's disease, and of parathormone, which saves the lives of patients with parathyroid tetany, both came from experiments on the dog. Many delicate surgical operations, such as the suture of blood vessels, operations on the heart, brain, lungs, and intestines were first tried on dogs. Also, many methods for the diagnosis of disease of the stomach, liver, gall bladder, etc., were developed by experiments on the dog. These examples should be sufficient to show that the humane experimental use of the dog is necessary and that incalculable good has come from such experimentation.

It is obvious to those who know medical scientists intimately that dogs would not be used unless their use was necessary and profitable. A medical scientist quite obviously in his teaching and research selects the animal deemed to be most suitable for the purpose.

Herman L. Kretschmer, Clinical Professor of Surgery, Rush Medical College, University of Chicago, Chicago: It is a well known fact that the span of human life has been increased about

eleven years, so that our expectancy of life is just that much longer than the life expectancy of our forefathers.

This great medical achievement is in a large measure the direct result of animal experimentation—so called vivisection. Many of the terrible epidemics that caused the deaths of millions of people have been practically wiped out, and this has been made possible only by animal experimentation.

I wish to confine my remarks only to that phase of vivisection that has resulted in saving the lives of millions upon millions of children all over the world. It is much better to secrifice the lives of any number of experimental animals rather than have one single child die.

One of the outstanding results of animal experimentation is the discovery of serums for the prevention and treatment of disease, and they play a very important rôle in the treatment of infants and children.

Diphtheria, that dreaded visitor in the home with children, has practically disappeared today. In Chicago, for example, in 1905 there were 2,220 deaths per 1,000,000. In 1933, there were only 2.5 deaths, per 1,000,000, from diphtheria. If the death rate of 1905 had existed in 1933, it would have meant that about 797 children would have died from this disease. In other words, 788 lives were saved as a result of knowledge gained through animal experimentation.

It might be well to emphasize the fact that these figures do not take into consideration the patient who suffers from diphtheria and, though he recovers, often has a permanent and an irreparable damage to his heart and kidneys, and leads a life of misery as a result of this disease.

It would seem that the animal experiments which resulted in the discovery of diphtheria antitoxin for treatment and the discovery and standardization of toxoid for the prevention justify this great saving—saving the lives and health of your children and mine.

The above story can easily be repeated when applied to the treatment of other diseases in infancy and childhood. May I call your attention to the almost complete abolition of rabies (hydrophobia), lock jaw (tetanus), cerebrospinal meningitis, and scarlet fever? The extensive and intensive study that is being directed to the dreaded disease of children, namely, infantile paralysis, cannot be undertaken without animal experimentation.

Vivisection does not mean cruelty to laboratory animals. These animals are given the best of food and care—far better care than that received by stray dogs, wandering up and down streets and alleys. Experimentation does not mean pain for the animal because all investigations are done under careful anæsthesia, and the care after operation is meticulous.

And, finally, may I call your attention to the fact that many humans have sacrificed themselves in the war against disease? For example, in the fight to discover the cause and method of the spread of yellow fever, there were brave men who permitted themselves to be inoculated with the germs of yellow fever to test the value of certain preventative measures against the dread disease. The number of doctors are legion who, in the study of cancer, have inoculated themselves with pieces of a cancerous tumor.

Who, then, could oppose the sacrifice of the lives of animals if it means progress in the battle against human disease, if it results in the prevention of epidemics, in the cure of many infectious diseases, and in the saving of countless human lives, and if it results in an economic saving to the individual himself and to the community as a whole?

RIGHT REVEREND WILLIAM LAWRENCE, Bishop of Massachusetts, Boston. Having been for some fifty years interested in the subject of vivisection, I have had occasion to notice various changes in the discussion.

The great improvement in the methods of vivisection has thrown into discard many of the earlier arguments and illustrations: for instance, Dr. Henry J. Bigelow, the Boston surgeon, used to be quoted as abhorring vivisection. I knew Dr. Bigelow. A keen surgeon, wonderfully rapid in his work, and of tender emotions, he shrank from such unnecessary cruelty as sometimes obtained in his day, but quotations from him today are anachronisms.

Recalling famous surgeons who have been vivisectors and have publicly upheld vivisection, I am impressed with their humane spirit and sympathy. It has always seemed strange to me that the members of the merciful calling of medicine and surgery should be held up to public scorn by the very citizens who turn to them when in illness or pain.

Of course in earlier days, vivisection was often cruel, necessarily cruel before the discovery of anæsthetics; but public opinion, the law, and the character of the men who in the course of their investigations practiced vivisection have revolutionized the methods, and in these past many years I have been amazed at the number of charges of cruelty and of illustrations which have been proved to have no basis of fact.

After all, is it not a question as to whether man shall or shall not use the lower animals (of course with all possible humane precautions) for the welfare of man?

At a hearing in the State House in Boston, President Eliot, being questioned, answered that it was the problem of the use of the lower animals by man for man's welfare, a principle which seems to be generally granted in our use of horses. "Indeed," he continued "we so use the cow who passes through the agony of childbirth and from whom her child is separated; she moans as a mother bereft of her child and all for what?" (and he turned to the protesting company) "that these ladies may have milk for their luncheon."

The whole question seems to me to simmer down to this: vivisection must be in some form if men are to be healed from disease and accident; methods must be as humane as possible. The final question is, shall we vivisect men, women, and children and thus learn how to treat other men, women, and children, or shall we with humane methods vivisect dogs, cats, rabbits, or mice in order that men, women, and children may be healed and live?

CLARENCE COOK LITTLE, Managing Director, American Society for the Control of Cancer, New York: During the past 20 years the emphasis in research on the nature and cause of cancer has shifted from a medical to a biological basis. The general consensus of opinion is that the change has opened up a number of new avenues of approach and has led us in the direction of increased knowledge and a clearer perception of truth.

Science has recognized the unique and absolutely essential part which animal experimentation has played and must continue to occupy in this field of research.

Nature has seen fit to afflict laboratory animals with many forms of cancer strikingly like those which occur in human beings. Nature has also given to such animals a far shorter life span than our own so that they attain the various "ages" at which certain types of cancer most commonly occur, in a few months or years—instead of in several decades as we do.

These facts have combined to make laboratory mammals an effective "short-hand" material for the purpose of research in cancer.

In view of the appalling death rate from cancer and because of its widespread incidence, research must not be hampered. The nature of cancer is such as to place almost staggering difficulties in the way of its analysis and control. Restrictive legislation of any sort concerning the use of animal material will definitely diminish and may finally preclude the chances of the conquest of this disease.

Only an eccentric, selfish, and over-emotional type of mentality can dare to attempt to obstruct science in its attempts to utilize fully every means at its disposal to learn more of the scourge which kills annually more than 120,000 of our countrymen. Those who circulate propaganda for such restriction of experimentation in cancer research should pause and ask themselves whether they care to become friends and allies of mankind's most sinister enemy.

ARNO B. LUCKHARDT, Professor of Physiology, The School of Medicine of the Division of Biological Sciences, University of Chicago, Chicago: As the result of animal experimentation there is available a general anæsthetic agent, namely, ethylene, whose anæsthetic properties could never have been discovered if animal experimentation had been denied to biologists and medical men. Ethylene is a gas which was found highly poisonous to flowering carnations and other forms of plant life. Since it was found present to a variable extent in illuminating gas, the investigators thought that its presence there might account in part for the harmful and deadly effects of illuminating gas when this latter gas is inhaled accidentally or with suicidal intent. Animal experimentation on the frog, mouse, rat, rabbit, guinea pig, cat, and dog showed that this gas ethylene given with oxygen was *not* poisonous to these animals. In fact, it put these animals to *sleep*. When the gaseous mixture of ethylene and oxygen was withdrawn the animals awoke seemingly none the worse for their experience. The investigators then inhaled the gaseous mixture themselves. The experience was pleasant. There were no after effects to indicate that the gaseous mixture, so poisonous to many forms of plant life, had the least degree of poisonous action. Further investigations showed that man, like the lower animals, was not only put to sleep but that in this sleep surgical operations were possible. At the present time it is one of the safest, if not the safest, of anæsthetic agents for human beings. Could the anæsthetic properties of this agent so useful to the surgeon and patient have been discovered in any other way than by animal experimentation?

FRED B. LUND, Surgeon in Chief, Carney Hospital, Boston: There are many important considerations which one should bear in mind before voting to restrict or hamper animal experimentation. First, let us consider universal epidemics

of small pox which used to devastate the world before vaccination and then remember that first inoculation and then vaccination were established, not by experiments on animals, but on human beings, who voluntarily offered themselves for new treatment in the hope, which has been justified, of saving mankind from this terrible scourge. Millions of human lives have thus been saved. Second, one might walk in retrospect through the wards of a city hospital before diphtheria antitoxin was used and watch the babies choke to death, in spite of all that could be done. A fearful sight it was, one which now is seen no more. Third, we should remember, that the discovery and preparation of diphtheria antitoxin was and is dependent upon experimentation on animals. Hundreds of thousands of innocent children have been saved from a horrible death by diphtheria antitoxin, and if you count the agony which their parents have been spared, it is hard to reckon the good that has been done. Fourth, let us consider the question of typhoid fever: If one walked through the military hospitals during the Spanish war, he saw thousands of the flower of our youth perishing of this deadly fever, but how different are the statistics of all the countries engaged in the World War. In this great war millions of men were involved, but they were all given inoculations, and we learn that a case of typhoid was the rarest thing in the world and that this dread disease hardly counted in the mortality statistics. In our great city hospitals today, typhoid fever is so rare that it is difficult to find a case to demonstrate to medical students. This means that thousands of lives have been spared and that an enormous amount of suffering, misery, and expense, has been saved for mankind. Such an improvement could not have been arrived at without the use of animals for experimentation and for the preparation of the serum. Fifth, let us think of tetanus or lock jaw, that scourge of surgical injuries and wounds which in all wars killed its thousands. In the World War antitoxin given as a routine for prevention so thoroughly stamped out tetanus that death from it was almost unknown. To be sure a few old worn out horses had to be kept in comfort in their old age, in order to have blood painlessly drawn from their veins to provide the serum, but that surely ought not to count for much in comparison with the enormous saving in human life, for before the use of antitoxin tetanus was fatal in 75 per cent of the cases.

It has been repeatedly demonstrated that doctors will give their own lives to increase knowledge. Think of Walter Reid! The question comes down to this, are the lives of a few dogs, cats, rabbits, and guinea pigs to be compared with that of thousands, hundreds of thousands of human babies?

The contributions of animal experimentation to surgery can hardly be estimated. Suffice it to say that the operation of transfusion of blood which had been attempted through the centuries, had to be worked out on animals before it could be applied in emergencies. The skill and delicate handling necessary to perform it could be acquired in this way alone. Only after such training could it be safely or effectively used in human beings.

All of the animals used in experiments do not die. Many of them live for many years under a loving care which they never would have had unless they had been fortunate enough to be selected for experimentation. All that are operated on at all are given anæsthesia. They do not suffer pain.

For which will you vote; for the lives of thousands of babies, or of a few dogs, cats, and rabbits painlessly sacrificed that men, women, and children may live? Will you allow hunting, which means the sacrifice of thousands of animals without anæsthesia, and prevent the painless sacrifice of a few animals, in order that thousands of our fellow human beings may be saved from death, and what is more, chronic painful disease?

Any public official who would choose the latter alternative has been described by the immortal English poet.

> "Man proud man, clothed in a little brief authority,
> Most ignorant of what he's most assured!
> His glassy essence like an angry ape
> Plays such fantastic tricks before high heaven
> As make the angels weep."

G. W. McCoy, Director, National Institute of Health, United States Public Health Service, Washington: The march of civilization is replete with invention and discovery, largely attained through empirical methods of learning. In applying these methods man has had to avail himself of the materials at hand, fitting the means to the end and holding himself ready at all times to change his basis of experimentation to one more promising.

In perhaps no scientific endeavor is this more evident than in medical and surgical research, where animals are used for experimental and test purposes, the ultimate trial taking place in man's own body. Much thought has been given and many efforts have been made toward devising satisfactory ways of studying certain diseases in lieu of animal experimentation. No physical or chemical processes have yet been found equal to

the biological approach to the solution of problems surrounding many of the pathological conditions of plants, animals, and man. Until such procedures are evolved there appears no choice, if a successful outcome is to be achieved, other than the use of animals in prosecuting medical research. And it cannot be denied that the results already accrued have been of such inestimable benefit to both man and animals as to justify a continuation of these methods.

GEORGE R. MINOT, Professor of Medicine, Harvard University Medical School, Boston: Much has been written concerning the benefits to mankind from animal investigation relating to infectious diseases. It is well known that modern medicine dates from the years 1865 to 1875 when Pasteur and Koch, through experiments upon birds and mammals, demonstrated that tiny organisms called bacteria were the cause of infectious disease. This led at once to the separation of infectious diseases into definite disorders caused by different kinds of bacteria. As further experiments progressed, it was found out that although these bacteria did harm, certain animals recovered. A study of the latter gave hints as to how to aid people suffering from special infections. Next in importance was the impetus given to surgery. The surgeon, having been shown by animal investigations how to kill bacteria, developed the methods of sterilization and discovered that wounds healed kindly if not infected.

But long ago it was recognized that only a fragment of illnesses is due to bacteria. Thus cancer and other tumors, gout, diabetes, pernicious anæmia, and such dietary deficiency diseases as scurvy and pellagra were obviously disorders of a different type. And, though it is not so generally recognized, animal investigation in relation to such diseases has been almost as fruitful as in relation to those disorders due to bacteria.

Thus diabetes, a terrible scourge due to an inability of the body to utilize properly sugar and similar foods, has been greatly mitigated by the discovery of insulin. It was known for a long time that if the pancreas, a gland in the abdomen connected with digestion, was removed from dogs, diabetes resulted. Many investigators studied this problem and several just missed its elucidation; and it was not until 1921 that Banting and Best finally extracted from the pancreas of dogs by a special method a substance, now known as insulin, which, when injected into the animals already made diabetic, relieved them of their disorder. Since that day thousands of sufferers from this malady have had their lives prolonged in comfort and must worship at the feet of those investigators and those animals whose work and sacrifice makes their living possible.

A somewhat similar story can be told of the relief to sufferers from pernicious anæmia, a disease heretofore always fatal, through the discovery that the feeding of animals' livers and liver extracts, or injection of the latter may maintain health for these individuals. Investigations on animals pointed out the effect of liver feeding upon growth, upon blood regeneration under certain circumstances, and had served to enhance essential knowledge concerning the blood. From such stepping stones combined with observations made during life and after death on various sorts of patients came the modern use of liver extracts and during their development animals were employed to determine if the products would be toxic for man.

The future solution of the cancer problem and many other conditions which are enemies to man in all probability will be solved in part by wise, judicious use of animal experimentation.

LOUIS D. MOORHEAD, Dean, Loyola University School of Medicine, Chicago: The use of animals is essential in the teaching of physiology and of surgery. In these subjects, even more than in chemistry or physics, the student must learn in part by doing work with his own hands. If a young surgeon were about to perform on my body his first major operation on a human being, I should be glad to know that he had passed a written examination on his surgery text. I should also be glad to know that he had watched experienced surgeons at work, had even held retractors and applied sponges for them. But I should be still further comforted by an assurance that he had himself successfully carried out, upon dogs, operations similar to that for which I was being prepared.

It is not necessary here to mention the contributions which have been made to medicine by experimental work on animals. Diphtheria antitoxin alone has saved thousands of lives. In modern times there has probably lived no greater benefactor of humanity than Pasteur. In an antivivisectionist state his career would have been cut short, for after the publication of his first animal experiments he would have been committed to jail.

Abolition of the use of animals would not only block further discoveries in medicine, but would make difficult or impossible the employment of several valuable drugs. Some of these, as smallpox vaccine and diphtheria antitoxin, require

living animals for their preparation; others, as insulin and viosterol, cannot be prepared in known strength by chemical methods, and must be assayed as to potency by trial administration to animals.

WILLIAM P. MURPHY, Instructor in Medicine, Harvard University Medical School, Boston: As one of the great army of dog and animal lovers among the medical profession, and as one vitally interested in alleviation of the illnesses and sufferings of humanity, I can scarcely overlook the great contributions to the healing art which have been made possible by our animal friends.

Even the physician in daily contact with sick men, women, and children cannot realize the myriad ways in which suffering is relieved and life prolonged through these contributions. How often the physician sees the almost miraculous return to life and then to economic efficiency through the use of digitalis in the patient whose heart muscle has been damaged or overworked and so fails to carry on its normal function. It has become possible to bring about such relief promptly, and with a degree of certainty, only through the accurate standardization of the effect of digitalis preparations by the use of cats.

Who can forget the hundreds of emaciated, sick little children who remained hopeless invalids and did not grow to maturity in the days before insulin became available? Rarely do we realize that much of our present knowledge of the use of insulin enabling diabetic children, as well as their fathers and mothers, to live happy, useful lives has been made possible through the aid of our dog friends.

It is impossible even to think of the many ways in which each of us has been relieved of or spared suffering even though we have not individually had the misfortune to be ill. Daily, patients are being aided through a critical attack of pneumonia as a result of the development of a serum; no longer do we have serious epidemics of smallpox or diphtheria; the victims of rabies, as the result of a "mad dog" bite, are no longer watched through an agonizing illness resulting in death. Daily, thousands are saved from invalidism or death through the skill and knowledge of our surgeons, made possible only through the intimate study of the animal anatomy and the effects of their procedures on animals which must of necessity be carried out as humanely and skillfully as they must later be done to save a human life.

In view of the great advances for the relief of human suffering which have only been possible through the study of animals in the laboratory and through the realization that the great body of medical men are lovers of animals, in particular, dogs, so that only the most humane methods are used in the laboratory, it is difficult to understand how a sane thinking individual cognizant of the sufferings of little children, men, and women can attempt to hinder further progress in the prevention and relief of this suffering.

WILLIAM H. PARK, Department of Health, Bureau of Laboratories, New York: At the present time we are deeply interested in making a vaccine which will produce immunity against poliomyelitis, a disease to which only the monkey and the human being are susceptible. To obtain such a vaccine, therefore, we must test it out in either the human being or the monkey. It is hard to believe that any one would suggest the use of children for such a purpose or that it would be used until we are perfectly certain that the vaccine will be safe and probably effective. Therefore, we have used more than 200 monkeys to determine the best methods of preparing the vaccine to test it for efficacy and harmlessness. Since completing our experiments, we have vaccinated some 30 children, all of whom have become immune and none of whom has suffered in the slightest from the injection.

Again, there is the question of diphtheria. Without the use of the guinea pig it would not have been possible to learn the value of diphtheria antitoxin, toxin-antitoxin, or of toxoid. Through the use of these animals we have been able to develop potent antitoxins and potent vaccines so that diphtheria is gradually being conquered. I understand from the health commissioner of Chicago, Dr. Bundesen, that there were only 7 deaths last year in Chicago from diphtheria. In this city there were only 86. Without the use of antitoxin we believe there would have been between 5,000 and 10,000 deaths. Could any thoughtful person really believe that it was not right to use these animals in this tremendous service to humanity? It may be of interest to know that these animals would never have been born under the best conditions and have been kept with such care for a number of months if they were not to be used for experimental purposes.

As is well known, a great deal of effort has been made to produce a vaccine to lessen the ravages of tuberculosis. It has taken several years of work and quite a number of rabbits to satisfy ourselves that the BCG vaccine does produce a definite amount of resistance in those vaccinated with it, and also that no danger will result from its use.

Our antipneumococcus serum which is giving such fine results in certain types of pneumonia can be standardized only by the use of white mice. Would any one having an attack of pneumonia doubt the value and the propriety of using white mice to standardize the potency of the serum, so that a proper amount might be given and the proper type of serum used?

For the production of the Pasteur treatment against the dreaded hydrophobia, the rabbit is the only means we have of producing the vaccine. Would any human being be willing to state that a person bitten by a rabid dog should not receive the vaccine because a rabbit had suffered death in its production?

I think these instances are enough to show the immense importance and the necessity of the use of animals in the perfection of serums and vaccines and for testing the potency of these serums and vaccines. Surprisingly little pain is given to the animals in our experimental work. Except for a few hours of actual distress before their death they suffer very little. It would be a great loss to the human race if those who are opposed to the use of animals for these purposes should make it impossible to carry on this work.

C. I. REED, Assistant Professor of Physiology, University of Illinois College of Medicine, Chicago: There is a great amount of medical knowledge that has been acquired by observation and deduction. Much of this type of information was acquired hundreds of years ago. But in spite of the ready availability of this knowledge in case of nearly all diseases, there was progress only to a certain point. Beyond this point no progress was made until experimental methods were adopted. To some extent the human patient may serve as a subject. But the experimental procedures that have yielded the most important knowledge are of such a nature that they cannot be employed except on animals.

No one will claim that all lines of experimental effort will lead directly to the cure of a disease. Some diseases may be controlled by purely empirical methods usually discovered by chance. Others may be controlled only by a rational comprehension of the underlying factors involved. Many experiments are undertaken solely for the purpose of acquiring this fundamental knowledge which is just as necessary in repairing the human body as for a mechanic to know the fundamental nature of a machine in order to repair it.

Our present knowledge of cerebral function was not possible until brain surgery on dogs was undertaken. The nature of cardiac function became apparent only after experiments were done on the hearts of many lower species. No progress was made in the control of many gastro-intestinal disturbances until experiments on animals revealed the fundamental functional processes involved.

The antivivisectionist says that our efforts have been useless because we cannot cure the common cold. The answer to this type of argument is that experimental investigation in human disease was not employed extensively until about a hundred years ago, whereas the experimental method was employed in other fields of science much earlier. If certain conditions have not yet been brought under control it means that we must do still more, not less, experimenting.

It would be quite as logical to say to the physicist, "You have not produced a perfect radio set, therefore you must stop the useless squander of time and money," as to insist that animal experiments cease because perfect results have not yet been secured.

PEYTON ROUS, The Rockefeller Institute for Medical Research, New York: Man has always striven to cure disease and prevent death. During thousands of years he could but look, guess, try, and slowly gather experience. Now, in the last two generations he has found out how to do more. Anæsthetics let him enter the living body without pain; and the precautions learned through experiments upon animals permit him to do so without danger. For the first time he can put his wits to work against disease by effectual methods. The most precious of these, proven such over and over, is animal experimentation. By looking inside animals, producing disease in them, and attempting its cure, physicians find out how both animal and human bodies behave and what to do when they are sick. They learn for the many by sacrificing the few. The facts already discovered have prevented countless children from choking with diphtheria, kept innumerable wounds from mortifying, alleviated heart disease, controlled pernicious anæmia, saved diabetics, provided means to avert distemper from dogs, and done away with important cattle, poultry, and swine plagues. Childbirth has been made safer, life easier and far longer, and the act of dying more tolerable. Yet living creatures still suffer too much and die too young. Is it not common sense to go on trying to help them by a method which has already yielded such gains? And common sense to utilize for the purpose the kind of animal required for new discoveries? No one wishes to experiment upon the dog. But the dog

is more than man's friend. He is man's near neighbor physicially. In his build, his diet, and the changes sickness produces in him he resembles man far more than do the other available creatures. Scientists could not have found out about some diseases, human and animal, had he not been experimented upon; nor can they do so in the future without him.

BELA SCHICK, The Mount Sinai Hospital, New York: The necessity of using animals for experimental medical purposes and the control of curative remedies is clear in the case of diphtheria. It was possible to study this dreadful disease, which is now under control, only by using guinea pigs and horses. Guinea pigs are the only animals which show the classical effect of the diphtheria toxin. They must be used if we want to know the virulence of the diphtheria bacillus and its toxin. In case of doubt as to whether a child is suffering with diphtheria or whether an individual is a carrier of innocent pseudo diphtheria bacilli or of real virulent diphtheria bacilli, the bacilli cultured from the throat must be examined. This examination can be made only by injecting guinea pigs. The decision in both cases is very important. In the first case it is essential to know if the child is suffering with diphtheria so that the patient may be treated with serum as quickly as possible. In the second example, the control of epidemics in families, schools, military units, and so on depends on the result. Diphtheria serum, which is necessary for the treatment of the disease, can be prepared only by immunizing horses with diphtheria toxin. Our entire knowledge of diphtheria has its foundation in the careful experimentation upon guinea pigs and horses. The Schick test, discovered by the writer, was made possible only by studies upon guinea pigs.

We should not forget that the study of diphtheria contributes only one of the pillars upon which rest the development of the fundamental laws dealing with immunity against infectious diseases. The discovery of diphtheria serum by Behring gave an impetus to further studies for combating infectious diseases. Every mother should be thankful that science has developed a method of immunizing her child against such a terrible disease as diphtheria and should also be thankful for the discovery of a treatment for the disease.

As a pediatrician, I am able to judge the progress which has been made in the knowledge of diphtheria and other infectious diseases endangering the lives of children. Also as a pediatrician, I am able to judge the enormous progress made by studying rickets and the manifold forms of avitaminosis in animals. All these studies result in the saving of the health of millions of children and adults.

All such investigations are made in well controlled laboratories. Nobody should make use of animal experimentation without there being an absolute necessity for it. But if I must choose between helping science in finding new remedies for conservation of health in treating disease on the one side, or sacrificing animals on the other, I cannot hesitate to use animals.

MAJOR G. SEELIG, Professor of Clinical Surgery, Washington University School of Medicine, St. Louis, Missouri: In this age and day, there ought to be no finer demonstration of carrying coals to Newcastle than a formal defense of the humane use of warm blooded laboratory animals for purposes of developing scientific and practical medicine. I, personally, am never more reverent than when I contemplate the blessings that have graced man's life as a result of the studies that have been made on lower animals. When I ponder over the fact that we have made an almost complete scientific conquest of diphtheria and typhoid fever, gained an incredibly broad understanding of tuberculosis, and gathered an untold wealth of information regarding infections in general; and when, further, I realize how many of the beneficences bound up with all this advanced thought have been won through the humane sacrifice of guinea pigs, I feel no more revolt of conscience than I do regarding the fatal annual migrations of millions of those other little rodents, the lemmings, when they voluntarily seek death in the sea. It was Disraeli who said that when he had to choose between monkeys or angels, he took his stand with the angels. In my turn, I say that if I have to choose between guinea pigs, dogs, and your and my children, I take the children as my preference.

There is no branch of the healing art that has not been strengthened as a result of properly conducted animal experimentation. It taxes patience to be reiterating this fact constantly. It is more important to realize the value of experiments on animals in attacking some of our up to now unsolved problems. Cancer is the greatest single killer among world diseases today, not even excepting primary heart disease. We do not know the cause of cancer; we know all too little about its cure. As one who is devoting all his limited and humble capacity to the study of this world scourge, I say with conviction that were we to be

denied the right to use the lower animals in our studies, our progress toward conquering this disease would be hobbled even beyond the realm of wishful thinking.

MAURICE B. VISSCHER, Head of the Department of Physiology, University of Illinois College of Medicine, Chicago: The basis on which the scientist asks for approval of his use of animals for research and teaching is that of common sense reason. The medical scientist asks that two major questions be answered in the light of actual human experience: First, is there indubitable evidence that animal experimentation has been of value in medicine and the other biological sciences, and second, is man justified in the humane use of lower animal life for his own welfare? These questions, it seems to me, can both be answered vigorously in the affirmative. Especially since Pasteur, Koch, Lister, Curie, and Banting, to enumerate but a few of the most prominent experimentalists, it is futile to deny that human happiness has increased due to specific discoveries based entirely on animal experimentation of various sorts. Regarding the ethical justification for employing animals for human ends, as long as our race uses meat, furs, leather, and feathers, as long as we domesticate animals as beasts of burden on farm and highway, and confine them as pets for our amusement and company, it would seem that no great differences of opinion actually exist regarding our right to use animals for human good. A few fanatics abstain from meat, but they are usually the most inconsistent ones in regard to confining animals as pets and beasts of burden. Until animals are given every privilege and sanctity accorded man himself there can be no argument on the ethical side.

As a worker in the medical sciences it is perhaps appropriate for me to add one further statement. From a study of the history of medical progress I am convinced that every major advance in modern medicine has depended either immediately or remotely, but in the latter case none the less completely, upon knowledge gained in animal experimentation. I stress the latter category because one frequently hears, even from within the medical profession, the statement that one or another great advance was made by study of the human directly. The last step is often, or one might say, must always be made by observations on man, but the background of knowledge has invariably been gained by experiments on animals, experiments which usually are of such a character as to preclude their performance upon human subjects.

OWEN H. WANGENSTEEN, Professor of Surgery, University of Minnesota Medical School, Minneapolis: Lady Mary Wortley Montague, who is frequently credited with having introduced inoculation against smallpox into western Europe, having observed the efficacy of vaccination in Turkey, wrote her friend, Sarah Criswell in England in April, 1717: "I should not fail to write some of our doctors very particularly about it, if I knew any one of them that I thought had virtue enough to destroy such a considerable branch of their revenue for the good of mankind."

This implied objectivity of the medical profession has been adequately set aside by the unselfish toil of physicians in their daily tasks and the fervent zeal with which medical men have sought the cause and cure of disease. Epidemics of plague, cholera, and other infectious diseases of one sort or another that have ravaged and decimated the population of the earth for centuries have been obliterated by the labor of love of physicians who have devoted their energies and consecrated their lives to the task of making this a better and safer world wherein to live.

This record of accomplishment has been largely possible through the medium of animal experimentation. The fetters of authority and tradition have been broken. The deception of rationalization on inadequate factual data has become generally recognized and the superiority of experiment over logic has been demonstrated beyond question. The value of hypotheses resulting from carefully made observations is appreciated, but the verity of such deductions must be weighed by the crucial test of experiment. Art without science is blind.

Much of our knowledge of the mode of operation of our digestive, circulatory, respiratory systems, and ductless glands is the result of practical tests upon animals. Similarly, the mode and means of the best therapeutic attack upon the diseases to which these viscera of man are heir has come about in large measure through animal experimentation. Those drugs which avail the most in the treatment of human ills have been discovered and their action and dosage determined through the agency of decisive trials upon animals. By the same means the pharmacopeia has been purged of reliance upon superstition and futile remedies in the treatment of disease.

Intelligent search for the cause and alleviation of disease must go on. One of the most valued instruments in this relentless inquiry is animal experimentation. Matters of such vital importance to health and happiness can not be left to chance. Biological research employing the scien-

tific method must continue; its discoveries and benefits are available to all men irrespective of creed or birth or whether rich or poor; through its agency more lives are saved than all the wars of all the ages have thrown away.

When man no longer slays animals for food or clothing or holds them subservient to his will, the significant value of truths learned in animal experiments will fully justify their performance for the protection and prolongation of human life.

### METHODS OF MEDICAL PROGRESS[1]

For a long time there has been need for a better understanding by the public of what constitutes animal experimentation. Unfortunately, for a great many years, the only information given to the public concerning animal experimentation came from the opponents of progress in medical science; their utterances contained many misstatements and much misinformation. Those who were engaged in the study of disease were, at first, too busy to realize that progress in medicine was being endangered by professional agitators. They did not know that laudable work was being falsely portrayed to an always credulous public. We are always quite willing to believe much that we read and hear and it so happened that for a long time the public read and heard a great deal about the so called evils of animal experimentation. At the same time the public was not informed of the tremendous positive benefits of such work and thus made able to judge for themselves whether or not experimental research was justifiable.

The word "vivisection," which is often used to describe animal experimentation, is an unfortunate one because it conveys a wrong picture to the mind of the average person. It does not begin to describe all that animal experimentation really is. It does not tell that the animals when used are rendered insensible to pain by an anæsthetic such as ether, the same as with patients in a hospital. It does not tell that, in those instances in which the animal is allowed to come out of the anæsthetic, just as great care is taken to insure the aseptic and cleanly performance of the operation as in human surgery. It does not tell that the animals used suffer far less discomfort and make much more rapid recoveries than do human patients. It does not tell that the animals in the laboratories are usually under less discomfort than those which undergo cutting operations at the hands of farmers in the barnyards or are killed in the slaughtering pens. Yet all these things are so.

[1]A compilation of material assembled from various sources.

Just what constitutes animal experimentation? In the first place, more than half of it consists of nothing more painful than a needle-prick for the purpose of injecting substances to determine their ability to produce disease and how they produce it. In either case, a great many of the animals so used never have any ill effects following the injection, nor do they succumb to the injection. In those that do succumb, death is no more painful than that due to natural causes. The other major phase of animal experimentation consists largely in the performance of operations much the same as those that human beings undergo daily in any hospital. These operations on animals have the added purpose of studying body functions, or of improving and perfecting methods that will save human lives later on. In these operations, the animals used are under complete anæsthesia and the requirements relative to cleanliness and technique are just as strict as in human surgery.

Animal experimentation embraces many different lines of study. Animals are used for studying the physiology of the vital organs of the body; they are used for studying various contagious diseases such as diphtheria, scarlet fever, smallpox, and a host of others. Animals are used for working out the details and perfecting the methods of various operations that may be used to advantage later on in human surgery; they are used for the determination of the suitable dosage of various curative drugs; finally, animals are used to a great extent in producing vaccines and antitoxins for the prevention and cure of contagious diseases in man and the domestic animals. For example, calves are used in the commercial production of smallpox vaccine. One calf will produce sufficient vaccine to protect several hundred thousand people against smallpox.

What is the purpose of animal experimentation? Primarily, its purpose is to find ways and means of conserving human life and the lives of domestic animals; of diminishing the pain of natural disease and making death more comfortable. This is brought about by teaching us more about the organs of the body in health and in disease; by studying the diseases of man and animals by means of reproducing them experimentally in animals; and by discovering methods of improving health and of preventing and combating disease.

Who does animal experimentation? It is carried on in various laboratories throughout the world, most of which are connected with medical and veterinary schools or agricultural experiment stations. These laboratories are in charge of specially trained, responsible men who stand high

in their respective professions and in their communities. These men are pledged to see that the work in their laboratories is carried on in a proper, humane, and careful manner. These men have dedicated their lives to the prolongation of human life and to the alleviation of suffering in man and beast. It should be noted that most investigators in research could obtain a greater financial return from work in less philanthropic fields, as the professions or business. It should be emphasized that the same major factors which have made modern surgery possible have also made modern animal experimentation possible: (1) discovery of anæsthesia, (2) discovery of bacterial origin of disease, (3) development of aseptic surgery.

The discoveries and applications in human medicine made possible by animal experimentation are innumerable; only a very few can be mentioned, as smallpox vaccination, diphtheria antitoxin, typhoid vaccination; the recent discovery of insulin which has so much value in treating diabetes; the recent discovery of the cause of scarlet fever and probable means for controlling it; the discovery of ethylene as a general anæsthetic; and the recent discovery of treating pernicious anæmia with liver. Added to these, there is the knowledge that has been obtained as to how the various body organs do their work and how they are affected in disease.

The saving of human lives by means of these discoveries is one of the brightest pages in medical history. Before the discovery of vaccination against smallpox, there occurred widespread epidemics of the disease which almost depopulated some communities. Today we rest in comparative security from the ravages of the disease because we have effective means of preventing it. Diphtheria used to be one of the most dreaded diseases and its toll of human life was large. Today, due to the discovery of diphtheria antitoxin, the death rate from that disease is negligible when the antitoxin is used promptly. In the Spanish-American war, typhoid fever caused the death of six times as many men as all other causes put together. In the World War, there was practically no typhoid fever for the very simple reason that a few years ago a vaccine was discovered which prevents the disease and today typhoid vaccination is a routine procedure in the armies, not only of our own country, but of other countries. In the United States army alone, it is estimated that no less than 30,000 of our boys' lives were saved by typhoid inoculation. Thus one might go on and recount innumerable instances of how the lives, not of hundreds, but of millions of people have been saved by discoveries that were made in laboratories using animals for observation.

Nor must we think that medical men have seen fit to use only the lower animals in their experiments. Time and again, doctors have volunteered as subjects in the study of certain diseases in which animals do not afford suitable media for the work. An instance is that of the American Commission appointed in 1900 to make an investigation of the deadly yellow fever in Cuba. It had existed perpetually in Havana, and occasionally it invaded this country, especially the southern states, where in one epidemic it caused the death of 15,000 persons. Yellow fever constituted one of the principal reasons for the French abandonment of the Panama Canal project. It had taken a toll of 22,000 workmen and no life in that pestilential zone was safe from it.

When the American Commission was appointed, no one had any clear proof either as to the cause of the disease or the means by which it was spread. As animals are not subject to yellow fever, it was necessary for men to volunteer. To make a long story short, it was found that yellow fever was spread by a certain variety of mosquito. A method of combating it was developed, but in so doing some of the doctors and private soldiers of the army who had volunteered as subjects gave their lives. They rendered an overwhelming service to humanity; then, the army, by wiping out the mosquitoes wiped out yellow fever in Havana forever.

Later, this discovery made possible completion of the Panama Canal by our own country, but only after the Canal Zone was cleaned up so far as yellow fever was concerned. In this connection it should be noted that while the character of the disease made it necessary to use the human for the experimental animal, the men doing the investigating, thus offering themselves, received their training in experimental research and had investigated and familiarized themselves with a comparable disease in the lower animals.

It must not be forgotten that progress in veterinary science has been similar to that of medicine, and animal experimentation is here also of the greatest value. Animal experimentation has furnished the basis for veterinary education; it plays a part in the production of about 10 per cent of the drugs used in veterinary medicine; it is concerned with 100 per cent of the so called veterinary biologic products. Much that the veterinary profession has been able to accomplish in the control of infectious disease has been due to animal experimentation.

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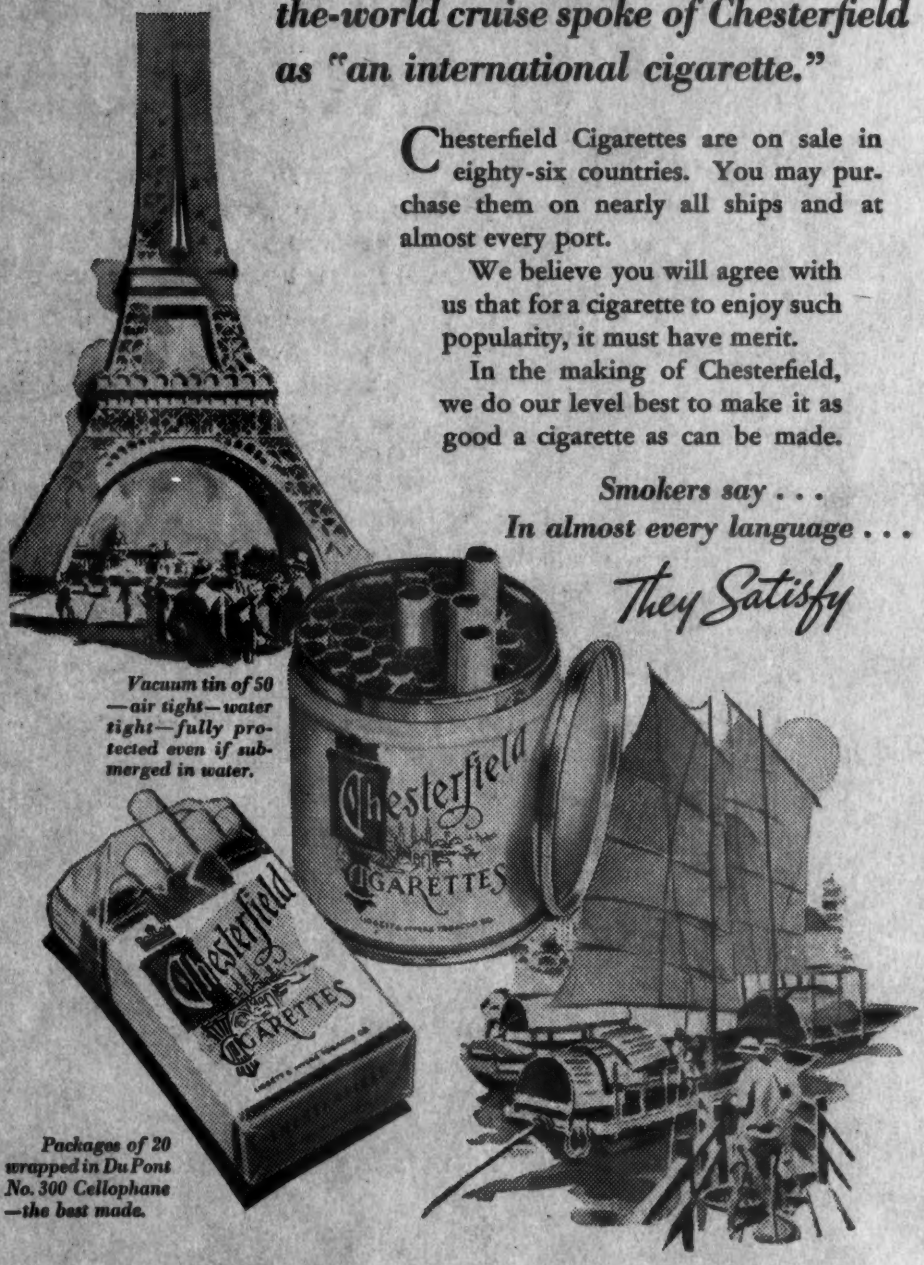


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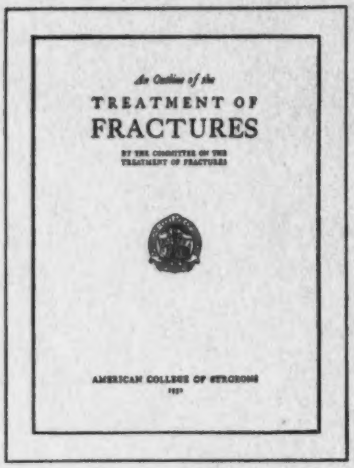


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